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THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE.*

FRANKLIN M. HANGER, JR., M.D.,
New York, N. Y.

Diseases of the liver often produce but few symptoms; and were it not for the frequent association of jaundice, a large number of hepatic disorders would escape clinical detection entirely. Yet, even after the patient has become icteroid, the physician is still confronted with the difficulties of determining whether the jaundice represents a benign disturbance requiring only reassurance, glucose and patience, or whether it is the harbinger of some serious malady necessitating difficult and often futile surgical procedures.

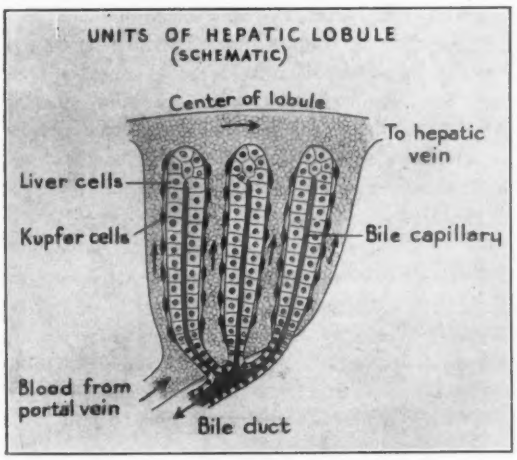

Fig. 1

Jaundice may be produced by a number of different physiological disturbances. These become more comprehensible by studying a functioning hepatic unit, i.e., one of the many cylindrical cords of liver cells, comprising a lobule. The terminal bile capillaries end blindly in this aggregate while surrounding them are the portal sinusoids lined by the Kupfer cells. Between the Kupfer cells and the liver cords lie potential spaces communicating with the lymphatic system. The functions of the cells of the liver parenchyma are numerous and are constantly being amplified with increasing chemical knowledge. They include both metabolic and excretory activities.

Metabolic activities—(1) Conversion of various carbohydrates into glycogen, (2) Deaminization of proteins and synthesis of urea, (3) Formation of serum proteins such as albumin and fibrinogen, (4) Fat and cholesterol metabolism (desaturation of fatty acids) (5) Maintenance of water balance, (6) Detoxification of drugs such as benzoic acid, phenol, camphor, (7) Utilization of vitamin K (naphthoquinone derivatives) in the elaboration of prothrombin, (8) Storage of the anti-anæmic factor, etc.

The excretory activity consists of the elaboration of bile which is chiefly composed of (1) bilirubin (bile pigment), (2) bile acids and their salts, (3) cholesterol and cholesterol esters, (4) excretion of various foreign colloids and dyes such as Congo red or certain phenolphthalein derivatives, (5) various enzymes such as phosphatase. It is not yet known if each liver cell is endowed with all these functions or if there is diversification among the various components of the lobule.

The Kupfer cells are unrelated to the liver cells embryologically. They are mesodermal in origin and form an important part of the reticulo-endothelial system. They are active in blood cell destruction and the conversion of hemoglobin into bilirubin. They also are highly phagocytic for foreign colloids in the circulating blood and play a role in antibody production and globulin formation.

Jaundice implies the accumulation of bilirubin in

*From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and The Presbyterian Hospital, New York City.

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the blood above 2 mg. per 100 cc. This pigment is a derivative of hemoglobin and is formed throughout the reticulo-endothelial system, spleen, bone marrow, lymph nodes where blood destruction normally takes place. Bilirubin appears in the circulating blood closely bound to the serum proteins until it is taken up by the Kupfer cells and passed on to the liver cells for excretion. Bilirubin before passing the liver threshold gives only an indirect Van den Bergh reaction. Once its union with serum complexes is disrupted by liver activity, a direct Van den Bergh reaction is obtained.

Jaundice can be discussed under three general headings: (1) Obstructive, (2) Hepatogenous, (3) Hemolytic.

OBSTRUCTIVE JAUNDICE

Obstruction to the outflow of bile from the liver leads to a rise of pressure within the biliary tree causing a back-flow or regurgitation of bile into the lymphatics and hence into the blood stream. Bile can be demonstrated in the thoracic duct a few hours after ligation of the common duct. In such cases dilatation and rupture of the terminal bile capillaries into the lymph spaces of the liver can be demonstrated histologically. It is noteworthy that although the liver cells may undergo gradual shrinkage and atrophy with long standing biliary stasis, they are not intrinsically diseased, hence liver function tests involving metabolic processes are usually but little impaired in cases of obstructive jaundice.

The causes of obstruction are numerous. Biliary calculi and inflammatory diseases of the gall-bladder probably account for over 70 per cent of all cases of obstructive jaundice. Carcinoma causes about 12 per cent. Inflammation of the bile ducts (cholangeitis) accompanied by swelling, scarring or spasm also produces obstructive jaundice as can swellings in the pancreas, enlarged lymph nodes, aneurysms, abscesses, and other pathological processes compressing the ducts. The jaundice accompanying biliary cirrhosis or neoplasm of the liver is essentially due to obstruction. It is said that occlusion of a few main hepatic ducts will not produce jaundice if the remainder of the liver is healthy.

HEPATOGENOUS JAUNDICE

The mechanisms of hepatogenous (non-obstructive) jaundice are less dependent upon mechanical factors. The commonest derangement of this type, catarrhal jaundice, was so named from the time honored assumption that the primary lesion was a duodenitis with ascending inflammation into the bile passages. It was assumed that the condition was essentially an obstructive jaundice produced by inspissated bile and swelling of the mucosal walls of the ducts. It was only during the last World War that Eppinger[1] had the opportunity of examining the livers of a number of jaundiced Austrian soldiers with this disease, killed in battle. He showed there was no obstructive process but necrosis of groups of liver cells in the lobule. With the dissolution of these cells the bile capillaries have open access to the peri-lobular spaces permitting a regurgitation of bile into the systemic lymph system. It is now generally agreed that catarrhal jaundice, in most instances, is in fact hepatitis and is seen in all gradations from mild icterus to fatal, acute and subacute yellow atrophy.

Many disorders can produce necrosis of liver cells leading to jaundice: chemicals—such as chloroform, phosphorus, arsphenamine, cinchophen and sulfapyridine; infections—(a) hepatotropic viruses, such as yellow fever, (b) spirochætes, as in Weil's disease or syphilis, (c) bacteria, such as paratyphoid, sepsis, and almost any severe systemic infection.

Some cases are supposed to follow food poisoning, others occur in epidemics. Many occur about ten days after an upper respiratory infection, as if it were a secondary toxic reaction in the liver such as is sometimes seen in the kidney after scarlet fever and other streptococcus infections.

In all events, the important factor is injury of the liver cells. They are sick and disintegrating in typical cases of hepatogenous jaundice. If injury is sufficiently severe and extensive, disturbances may be observed in some of the liver functions already mentioned. Theoretically these tests should distinguish obstructive jaundice from the hepatogenous variety but in actual practice most liver function tests have been rather disappointing.

In some instances toxic and obstructive factors may co-exist in producing jaundice. Bile casts in the biliary capillaries have been described in cases of catarrhal jaundice. Also the œdema and swelling and cellular infiltration accompanying hepatitis may cause an intrahepatic biliary stasis.

HEMOLYTIC JAUNDICE

This condition occurs when the liver is unable to eliminate the products of blood destruction, either because of excessive red blood cell breakdown or

because of derangements of the Kupfer cells, or both.

It is encountered most commonly in patients with a congenital defect in red cell morphology. Small spherical cells are present which disintegrate in relatively high concentration of salt solution (0.7 per cent —complete 0.5 per cent) and also are destroyed rapidly by the spleen, causing excessive amounts of hemoglobin derivatives to be eliminated by the liver. A variety of conditions bringing about undue blood destruction, such as faulty transfusions or hemolytic poisons, can produce the same effect. Hemolytic jaundice is easily recognized, especially when due to congenital spherical microcytosis.

TABLE I

DIAGNOSTIC FEATURES OF HEMOLYTIC JAUNDICE

(1) Jaundice frequently of long duration without malaise, itching, bradycardia, or bleeding tendency.
(2) Often a familial incidence.
(3) Enlargement of spleen.
(4) Hyperchromic, microcytic anaemia in familial type.
(5) No bile in urine. Urobilin increased.
(6) Stools darker than normal.
(7) Increased fragility of red cells in familial cases. Fragility normal in acquired type.
(8) Serum bilirubin increased rarely above 10 mg. per 100 cc.
(9) Indirect Van den Bergh.
(10) Tendency to gall-stone formation.
(11) Familiar cases cured by splenectomy. Acquired type not benefited.

The problem of major clinical importance is to distinguish obstructive jaundice from that due to inflammatory and degenerative processes in the liver parenchyma. When obstruction is the cause, prompt surgical intervention is usually indicated as patients are better operative risks; the duration of the illness can be shortened; the tendency to hemorrhage has not yet developed; and if a neoplasm is present, the opportunities for complete extirpation are improved. On the other hand, if jaundice is due to disease of the liver, a general anaesthetic and operative trauma are definitely harmful and may actually precipitate a fatal outcome.

Since the introduction of vitamin K therapy in the pre-operative treatment of the icteric patient, a difference of considerable practical importance has been noted in the two types of jaundice. Hemorrhagic tendency develops in the obstructive group because bile salts, necessary for the absorption of vitamin K, are absent from the intestinal tract. Clotting time of patients with biliary obstruction decreases rapidly following the daily oral administration of 2,000 units of the vitamin with two to three grams of bile salts. In cases of hepatogenous jaundice, the bleeding tendency is not due to faulty absorption of vitamin K but rather to inability of the injured liver to utilize the vitamin in prothrombin formation. These cases often fail to respond to routine treatment and hence are subject to greater operative risk.

The differentiation of these two types of jaundice may be extremely difficult. It is often found expedient to treat the jaundiced patient conservatively at first, but if no spontaneous improvement takes place within a six-week interval, exploration is recommended to establish a diagnosis. But, in our experience, watchful waiting of this kind is seldom necessary if certain clinical features and laboratory procedures can be evaluated properly.

CLINICAL DIFFERENTIATION

The clinical features of possible diagnostic value (Table II) are based chiefly upon an analysis of 235 jaundiced cases seen at the Presbyterian Hospital and reported by Flood and associates in 1933.[2] Few comments are indicated:

Age is an extremely important consideration. It is very reassuring when the jaundiced patient is young, for benign hepatitis is usually present and acute yellow atrophy seldom develops. Stone or carcinoma are unlikely. The great difficulty is recognizing hepatitis in patients after forty. It is in this group that unnecessary operations are often performed.

Sex is of little diagnostic aid except in differentiating carcinoma of the pancreas from that of the gall-bladder. Symptomatically these may be indistinguishable.

Initial symptomatology in many instances determines the duration of jaundice before the physician is consulted. Patients with catarrhal jaundice are sickest at the onset, while neoplastic obstruction may be so insidious that the patient is not alarmed. The patient with gall-bladder disease, on the other hand, may be so accustomed to G.I. upsets that he postpones professional aid until self-medication has failed.

The presence of pain is important as it frequently leads the clinician into error. Contrary to current teaching, pain and tenderness of the liver is not uncommon in hepatitis. I have seen numbers of patients explored needlessly because this was the strik-

TABLE II

CLINICAL FEATURES OF POSSIBLE VALUE IN DISTINGUISHING HEPATOGENOUS FROM OBSTRUCTIVE JAUNDICE

	Hepatogenous Jaundice (Medical)	*Obstructive Jaundice* (Surgical)	
	Catarrhal Jaundice, Acute Yellow Atrophy, Arsphenamine Jaundice	Carcinoma of Pancreas, Gall-Bladder, Bile Ducts and Liver (primary)	Calculus in Common Bile Duct
Age	80% under 40 years	80% over 40 years	80% over 40 years
Sex	Catarrhal jaundice 67% males Acute yellow atrophy 76% females	Ca. of pancreas 72% males Ca. gall-blad. usually female	71% females
Initial Symptom	Anorexia, nausea, vomiting or malaise 60%	Pain 48% Insidious jaundice 27%	Preceding indigestion Jaundice intermittent or recurrent
Upper Abd. Pain	Present in 56%	Present in 65%	Present in 97%
Upper Abd. Tenderness	Present in 55%	Usually absent	Present in 29%
Itching of Skin	Often absent, usually mild	Usually present except with primary carcinoma of liver	Often absent
Loss of Weight	Not striking	Average 20 pounds	Usually
Prodromal Upper Resp. Infection	Present in 25%	None	None
Fever	Often present	Often present except with carcinoma of the pancreas	Often present
Spleen	Often palpable or enlarged by X-ray	Not palpable	Not palpable
Diabetes Mellitus	Absent	With carcinoma of pancreas develops in 23%	Absent

ing symptom. On the other hand, it is important to recall that 5 per cent of stones in the common duct are symptomless and are usually mistaken for malignancy. Obviously all patients with persistent obstructive jaundice are entitled to exploration even if the chances of finding a silent stone are slight. Carcinomas of the pancreas and gall-bladder are usually not painless, as is generally taught.

The *spleen* should be carefully studied in all cases of jaundice. When enlarged, the diagnosis of hepatitis can be made with reasonable assurance. Hepatitis and cirrhosis, however, are not always accompanied by splenomegaly but the association is so common that an X-ray to determine splenic size may be expedient when this organ is not palpable.

Severe *itching* is an important differential feature favoring obstructive jaundice. It may even precede the visible jaundice.

Other features of little aid are the *size of the liver*, which is usually enlarged in all cases except acute yellow atrophy. *Fever* which may or may not occur with hepatitis or obstructive processes. *Dilated gall-bladder* may be misleading, as clinically it is often impossible to distinguish it from a lobe of the liver. Mistaking the gall-bladder is one of the commonest sources of diagnostic error. *"Amine breath"* and *drowsiness* occur more commonly in severe hepatitis.

In summary, the age of the patient, the presence or absence of severe itching and the palpability of the spleen, are the most valuable clinical features in distinguishing obstructive jaundice from that due to hepatitis.

LABORATORY DIFFERENTIATION

In Table III are indicated a variety of investigations which may be carried out in cases with jaundice. It has been implied that liver function tests theoretically should detect disturbances of the liver parenchyma, thus distinguishing obstructive jaundice from that secondary to liver disease, but actually these can be very misleading as considerable liver damage may be present with normal function tests. Also one function may be impaired out of proportion to the others, and, furthermore, few tests are sufficiently delicate to be dependable in border-line cases.[3, 4]

Bile in Stools. Bile may be absent in hepatitis for many days but usually reappears. Stools should be examined frequently as they usually remain permanently acholic if the occlusion is due to neoplasm.

Serum Bilirubin. This is a more accurate index of the severity of the jaundice than the patient's color.

TABLE III

LABORATORY PROCEDURES OF POSSIBLE DIAGNOSTIC VALUE IN DISTINGUISHING HEPATOGENOUS FROM OBSTRUCTIVE JAUNDICE

Test	Normal Values	*Hepatogenous Jaundice* (Medical)	*Obstructive Jaundice* (Surgical)	
		Catarrhal Jaundice, Heptatitis, Etc.	Carcinoma of Pancreas Carcinoma of Gall-Bladder Carcinoma of Bile Ducts	Calculus in Common Bile Duct
Bile in Stools	Present	Intermittent	Persistently absent	Intermittent
Serum Bilirubin	1 mg. per 100 cc. or less	Often marked increase Rapid rise	Often marked increase Gradual rise	Moderate increase
Icteric Index	8 or below	Average 144	Average 116	Average 61
Van den Bergh	Indirect	Direct	Direct	Direct
Duodenal Drainage — Bilirubin	Present	Rarely completely absent Light color	Absent	Rarely completely absent. Dark color
Duodenal Drainage — Microscopic	No crystals or pus cells	May be pus and hepatic cells	Negative	Clumped cholesterol crystals and pus cells
Duodenal Drainage — Bacteria	Usually sterile	Variable	Negative	Colon bacilli 65%
Blood Cholesterol Total	150-220 mg./100 cc.	Usually normal Av. 178	Often elevated Av. 339	Often elevated Av. 282
Blood Cholesterol Esters	80-120 mg./100 cc.	Usually reduced Av. 65-90	Normal	Normal
Galactose Tolerance Test 40 gms.	Less than 3 grams excreted in 5 hours	Impaired (6-8 gms. in 5 hours)	Normal	Normal
Bromsulphalein (5 mg. per kilo)	No retention after 30 min.	Impaired excretion	Impaired excretion	Impaired excretion
Serum Phosphatase	Less than 4 Bodansky units	Usually below 10 units	Usually above 10 units	Usually above 10 units
Cephalin-Cholesterol Flocculation	Negative	Positive	Negative	Negative

The rise or fall of the serum bilirubin is the best method of following the patient's course and often is the deciding factor whether to operate or continue conservative therapy.

Icteric Index is another method of determining the bile in the serum by comparing the intensity of yellow with a standard potassium bichromate solution. It is simple but less reliable than the serum bilirubin determination, as other pigments (carotin) or laked r.b.c. may give misleading results.

Van den Bergh reaction is valuable only in distinguishing hemolytic jaundice. All efforts to refine this test into delayed and diphasic types are useless in distinguishing obstructive from hepatogenous jaundice.

Duodenal Drainage is perhaps more accurate than stool examination in determining if there is flow of bile. The material can be studied in a number of ways which may be helpful in differential diagnosis, i.e., microscopic and culture.

Blood Cholesterol. The liver probably synthesizes cholesterol esters and maintains a constant ratio between free cholesterol and cholesterol esters in the blood. In obstructive jaundice cholesterol may be increased. In liver damage the esters may be low. This method is still employed but less enthusiastically than formerly.

Galactose Tolerance Test and the *Hippuric Acid Test* are probably the best of the liver function tests, but even these are often not satisfactory as the variables of the methods preclude accurate interpretation of slight deviations from normal readings.

Bromsulphalein is a measure of hepatic excretory function. In cases of jaundice of all types the elimination of dyes may be impaired. Naturally X-ray visualization of the gall-bladder of the jaundiced patient by tetraiodophenolphthalein is of little use, as this dye also may not be excreted by a damaged liver.

In our clinic the *Serum Phosphatase* is regarded as one of the most valuable methods in detecting obstructive jaundice. Phosphatase is an enzyme which originates in the bone producing cells. It escapes into the blood and is eliminated from the body in the

bile. It is detected chemically by its capacity to split organic phosphates such as glycero-phosphate into inorganic phosphate. When there is biliary obstruction the phosphatase rises promptly in the blood (reaching values as high as 113). In hepatitis there is usually but little increase. The value of this test has been reviewed recently by Gutman in our clinic (Table IV) who has shown that the two main types of jaundice can be distinguished readily in most instances.[5] Our surgeons hesitate a long time before they will consent to operate on a case of jaundice with a phosphatase under ten units.

TABLE IV

SERUM PHOSPHATASE VALUES IN BODANSKY UNITS (NORMAL 1-4) IN MAJOR DISORDERS OF LIVER AND BILIARY TRACT—308 ADULTS

DIAGNOSIS	TOTAL NUMBER OF CASES	4 OR LESS	4.1-9	9.1-12	12.1-25	25+
Occlusion of Common Bile Duct	79	0	6	10	46	17
Catarrhal Jaundice	69	8	48	8	4	1
Jaundice after Hepatotoxic Drugs	38	2	18	4	13	1
Hepatic Cirrhosis (non-biliary)	44	14	20	5	4	1
Hemolytic Jaundice	13	13	0	0	0	0
Neoplastic Involvement of Liver	47	4	18	5	18	2
Liver Abscess	10	0	2	3	3	2
Chronic Passive Congestion of Liver	8	3	5	0	0	0

—Courtesy of Dr. A. B. Gutman, College of Physicians and Surgeons.

The disadvantages of the serum phosphatase determination as a diagnostic procedure in hepatic disorders are—(1) It is not a simple technique and, unless scrupulous care is used in the laboratory, erroneous results are obtained. (2) It is elevated in certain bone diseases such as hyperparathyroidism, Paget's disease, rickets, bone metastases, etc. (3) Children with obstructive jaundice show a surprisingly small increase. (4) High values may be obtained if there is non-surgical intra-hepatic obstruction such as carcinoma.

The *cephalin-cholesterol flocculation* test is of special interest to me, for, while working on some unrelated immunological problems, I happened to observe that emulsions made of cephalin and cholesterol flocculate in the presence of serum from patients with inflammation and disintegration of liver parenchyma, but remain stable in normal serum or in the serum of patients with obstructive jaundice. The technique as now employed has been recently described.[6, 7] It consists essentially of diluting 0.2 cc. of the patient's serum with 4 cc. saline to which is added 1 cc. of an emulsion of cephalin and cholesterol. Readings in terms of plus are made after forty-eight and indicate the degree of flocculation. Complete precipitation of the emulsion is designated as ++++. This test has been performed on more than a hundred cases of hepatitis and has been found definitely positive in about 90 per cent of instances. On the other hand, a comparable number of cases of proven obstructive jaundice have given negative or weak reactions in almost every instance.

The significance of the reaction is still being investigated. We have been able to show that flocculation depends upon a specific reaction between the colloidal cephalin and a globulin fraction which appears in the serum when there is active irritation of liver cells. It is not a liver function test but rather an index of irritation of this organ, and can be employed clinically to detect active disturbances in the liver somewhat as albuminuria denotes disturbances within the kidney.

Like all other laboratory procedures, the test is not infallible. The chief factors discovered to date which require caution are—(1) It has not been established beyond doubt that other diseased organs besides the liver may not elaborate flocculating substances. Globulin *per se* will not produce flocculation. (2) It is impossible in certain instances to differentiate intra-hepatic obstruction requiring no surgery from obstruction of the large bile ducts. The flocculation test should be used in conjunction with serum phosphatase determinations. (3) The test may become negative in hepatitis before the jaundice has subsided completely. (4) The cephalin employed must be standardized. Freshly prepared cephalin may be too delicate and show slight flocculation with presumably normal serum.

CONCLUSION

Let me emphasize in closing that there is still no single procedure infallible in the differential diagno-

sis of hepatogenous from obstructive jaundice. Careful study of the case along the lines I have indicated will usually clarify the problem, but each bit of data must be carefully evaluated. In this age of growing laboratory omnipotence, clinical judgment is still the primary requisite when disorders of the liver are under consideration. It is still necessary to employ, as best we may, scientific understanding, patience, and eternal vigilance.

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620 West 168th Street.

THE PRESENT STATUS OF OUR KNOWLEDGE CONCERNING PITUITARY DISEASE.*

J. M. MEREDITH, M.D.,
Department of Neurological Surgery, University of Virginia, C. C. Coleman, M. D., Director, University, Virginia.

Introduction. From time to time, it is of considerable value to consolidate and summarize our knowledge of any important subject in medicine in order to manage more effectively the patients who present themselves for relief. It is with the hope of clarifying our present information concerning pituitary disease, following a review of the literature and the inclusion of certain pertinent data from the neurosurgical clinics of the University of Virginia and the Medical College of Virginia, that this presentation has been prepared.

OUTLINE

PART I—EXPERIMENTAL EVIDENCE

1. Historical
2. *Development* and *Structure* (from hormonal standpoint)
3. *Physiology*
   - A. Known Hormones from anterior lobe (growth and sex)
   - B. ? Hormonal influence of posterior lobe
   - C. Pars intermedia (of buccal origin and hence glandular)
   - D. Associated vegetative centers of the Diencephalon
   - E. Reciprocal action of endocrine secretions
   - F. Anti-hormone theory

PART II—CLINICAL CORRELATION

1. Clinical types of pituitary disease
   - A. Fröhlich's Syndrome
   - B. Giants and Acromegalics
   - C. Cushing's Syndrome
   - D. Chromophobe Tumors
   - E. Craniopharyngioma
   - F. Simmonds' Disease
   - G. "Mixed" Types
   - H. Diabetes Insipidus
   - I. Pituitary Dwarfs and the Lorain Syndrome
   - J. Laurence-Biedl-Moon Syndrome
   - K. *Miscellaneous:* (carcinoma, gumma, tuberculosis)
2. Therapy—Other than Hormonal—of Certain Lesions Described Above (Part II).

PART III—PITUITARY ORGANOTHERAPY

1. *Anterior Lobe*
   - (a) Growth Hormone
   - (b) Sex Hormone

*Read at the Symposium on Endocrine Diseases, University of Virginia School of Medicine, April 29, 1938, and at a General Staff Meeting, University of Maryland Hospital, Baltimore, November 20, 1939.

(c) Effect of antuitrin on myasthenia gravis
(1) Analogy to Simmonds' Disease

2. *Posterior Lobe*

A. Pituitrin
1. Oxytocin
2. Pitressin

Conclusions: (In Reference to Organotherapy).

PART I—EXPERIMENTAL EVIDENCE

1. *Historical:* The pituitary gland and its adjacent structures in the region of the circle of Willis inspired the curiosity of Galen, Andre Vesalius and other early anatomists who gave it uncertain hormonal properties.

Attention was recentered on this gland by the French neurologist, Pierre Marie, who, in 1886, described a curious malady of hypertrophic skeletal changes in the adult which he called, appropriately enough, acromegaly.[1] It was observed sometime later that there was an associated hypophyseal tumor. Led by Cushing,[2, 3] the evidences of pituitary hypo- and hyper- function have slowly but steadily been elucidated and, during the last few years, the *hormonal properties* of the gland have been investigated by a veritable army of workers. Still other functions have been ascribed to it until today it is recognized that growth, nutrition and reproduction, the basic functions of life, have their center here. Truly, the pituitary gland is the keystone of the endocrine arch.

2. *Development and Structure:* The anterior lobe of the pituitary is derived from the buccal mucosa and is made up of three cellular elements: the chief or mother cell is the (a) *chromophobe* which, in the process of maturing, acquires coarse secretory granules that stain deeply—the *chromophile* cell. These two types exist in about equal proportion. But the chromophile cells can be further divided into those whose granules take the acid dye (b) *acidophilic* and those whose granules take the basic dye (c) *basophilic.* These latter two groups of cells exist in a proportion of 4:1.

The posterior lobe is derived from the diencephalon—or interbrain—surrounding the third ventricle, and is made up of cells of glial—not glandular—origin as well as fine myelinated nerve fibers which descend from the diencephalon by way of the infundibulum to end in a plexiform arrangement in the posterior lobe. There is no glandular arrangement of cells in the posterior lobe and the blood supply is scant. But there are certain hyaline structures, known as Herring bodies, scattered throughout the posterior lobe, thought to have secretory properties; these eventually migrate into the lumen of the third ventricle via the infundibulum to the floor of the third ventricle. It was thought by Cushing[3] that these hyaline bodies found in the posterior lobe originate in the pars intermedia—which latter structure is also glandular in origin, arising from the original buccal outpouching—and that they constitute the active principles of pituitrin—the posterior lobe secretion.

The posterior and anterior lobes have *individual* arterial supplies independent of that of the vegetative centers in the hypothalamus. The anterior lobe is drained by veins leaving its lateral borders to enter the adjacent cavernous sinuses. No veins have yet been found draining either lobe via the stalk to ultimately reach the hypothalamic vegetative centers in the floor of the third ventricle.

3. *Physiology:*

A. *Anterior Lobe.*—There are two powerful hormones derived from the anterior lobe; (a) the *growth* hormone and (b) the *sex* or gonadotropic hormone, both originating from the chromophile cells of the anterior lobe. Furthermore, there is fairly convincing proof that the growth-promoting hormone is formed by the acidophilic cells and the sex hormone by the basophilic cells.

The rat has been found by Smith[4] to be ideally suited to hypophysectomy because the body of the gland, as in the human subject, is covered by a dural diaphragm and can readily be removed without damage to adjacent hypothalamic structures. Thus in the rat an exact state of apituitarism can be produced, thereby allowing the testing of the effects of replacement therapy.

If the pituitary be removed in a *young* rat, retardation in growth and failure to mature sexually occur and the animal resembles a delicate dwarf.

If the pituitary be removed in a *sexually mature* rat, there result a progressive loss of weight, a degeneration of the genital system characterized by atrophy of the gonads and immediate cessation of estrus in the female, together with atrophy of the thyroid, parathyroid and suprarenal cortex. The basal metabolic rate is lowered.

If fresh hypophyseal tissue be now transplanted intramuscularly into these animals from normal rats, the dwarf grows, and matures sexually; in the adult, estrus returns, genital atrophy disappears and the

associated endocrine glands recover their former structure.

Furthermore, these regressive changes do not occur if the posterior lobe *alone* is removed; it, therefore, appears that the anterior lobe *alone* is entirely responsible for growth and sexual maturity.

Not to be confused with the gonadotropic hormone of the anterior pituitary (q. v. supra) is the *male sex hormone,* an entirely different substance, found in *testicular tissue.*

Brief mention only will be made of *other* hormones from the anterior lobe which influence the activity of the thyroid, adrenal cortex, parathyroid, secretion of milk and metabolism of fat and carbohydrate. An hematopoietic hormone has been demonstrated experimentally by French workers.[5] Much of what was once thought to be the direct influence of hypophyseal secretion is now known to result from secretions of other endocrine glands *activated* primarily by the pituitary gland. Thus the terms: thyrotropic, corticotropic, parathyrotropic and pancreatropic hormones of the pituitary gland.

B.? *Hormonal Influence of the Posterior Lobe.* The hormone of the *posterior* lobe is known as pituitrin and from it have been obtained pitressin and oxytocin. Howell[6] was the first to point out that the rise in blood pressure after injection of pituitary extract occurred only after an injection of *posterior* lobe extract.

Pitressin elevates the blood pressure and slows the heart rate; it is less marked in effect than epinephrin but its effect lasts longer. Pitressin also stimulates smooth muscle generally. It produces diuresis in the normal subject. Pitressin stimulates the flow of milk, i.e., a galactogogue—which it accomplishes probably by stimulating the smooth muscle of the breast rather than the secreting cells themselves.

Oxytocin contracts the uterine musculature for which it has a specific action.

What we are interested in particularly at this point of our discussion is whether or not there is convincing evidence that the *posterior lobe* is a gland of internal secretion. Van Dyke[7] concludes that despite the apparent wealth of evidence in favor of the posterior lobe as a gland of internal secretion, closer examination of the experimental data reveals that the evidence is unsatisfactory. The most numerous experiments—those in which oxytocic effects have been studied—are the least satisfactory. The demonstration of vasopressor or anti-diuretic effects by blood or cerebrospinal fluid or by extracts of these is, in itself, suggestive, but does not prove that the effects demonstrated are due to the active principles of the posterior lobe. Vasopressor substances which are pharmacologically different from that of the posterior lobe can be extracted from both the blood and the cerebrospinal fluid. Finally, an anti-diuretic substance, differing from that of the posterior lobe, has been extracted from the *liver* according to Theobold and White.[7]

C. *Pars Intermedia.*—Van Dyke[7] states that nearly all experiments in amphibia show that the pars intermedia elaborates an internal secretion which causes a dispersion of the black pigment granules in the epidermal melanophores. It may be concerned with visual adaptation in mammals.

D. *Role of the Diencephalon.*—Functions previously ascribed to the hypophysis are now known to depend on vegetative centers of the diencephalon. Water balance, fat and carbohydrate metabolism are the principal processes concerned in this dual relationship, as are heat regulation and pathological sleep. Not all pituitary hormonal action is blood borne to other endocrines; it may be by direct diencephalic action instigated by pituitary hormones.

The diencephalon or interbrain—so-called because it lies between the end brain or telencephalon and the midbrain or mesencephalon — surrounds the third ventricle.

The most striking somatic change which has been produced by injury to or disease of the hypothalamus is extreme adiposity (Fig. I). This may be brought about without injury to the hypophysis. An entirely parallel condition is seen clinically, following injury or inflammation of the region of the tuber cinereum. It is a well-recognized sequel of epidemic encephalitis (i.e., adiposity). The condition often is mistaken for disease of the hypophysis.

We know that a mild temporary increase in water metabolism may follow removal of the hypophysis but its degree and persistence cannot be compared with the results of some lesions of the tuber cinereum which do not affect the contents of the sella. Diabetes insipidus may be due solely to hypothalamic disease (Table I). There is, furthermore, pathological evidence that a number of other disturbances, such as somnolence, narcolepsy and vasomotor changes may be produced by lesions of the floor of the third ventricle in which lies the tuber cinereum. This

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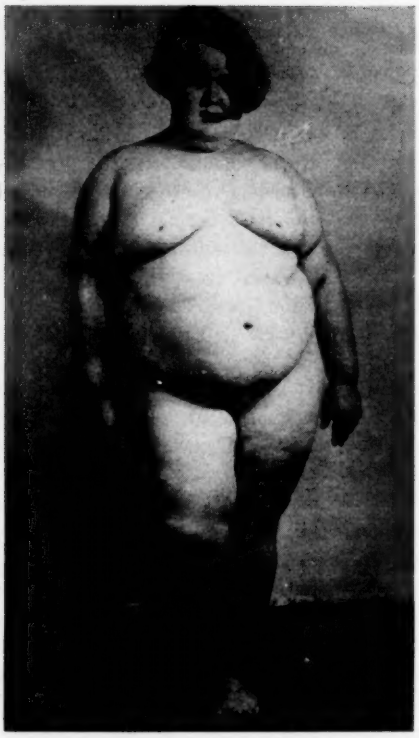

Fig. I.—Ten-year-old child. Normal fundi. Sella normal. No diabetes insipidus. Menses not yet established. Adiposity may be due entirely to diencephalic disease. (Possibly associated anterior pituitary hypofunction. See Table I.)

fact is mentioned here only because these manifestations have also been attributed to disturbances of the hypophysis alone.

In internal hydrocephalus, the hypothalamic or diencephalic region may become reduced to paper-thinness and in the course of operations on tumors of the third ventricle it may be severely damaged and yet none of the symptoms just enumerated may appear. The explanation of this contradictory situation has not yet been suggested.

E. *Reciprocal Action of Endocrine Secretions.*—Hormonal actions of the pituitary are not always one direction, i.e., not invariably from the pituit to other organs. Ovarian hormones in pregnan have been known to produce enlargement of th pituitary to the point of causing a bi-temporal hemianopsia and pituitary headaches, and that *ovarian* secretions may unfavorably influence the hypoth amus is demonstrated by the well-known tenden of women to gain considerable weight after one or more pregnancies. This is known as the *reciproca action of endocrine secretions.*

F. *Anti-Hormone Theory.*—One more variation in the hormonal doctrine of endocrinology is t *anti-hormone theory.* Following prolonged treatm with certain pituitary extracts, there is a progressiv diminution of their effects. This is ascribed to the formation of *anti-hormones.* Collip[8] believes that anti-hormones are found in a yet unlocalized portion of the body and antagonize the pituitary hormones.

PART II. CLINICAL CORRELATION

1. *Clinical Types of Pituitary Disease:* Most of these syndromes, as recorded in the outline (q. v. supra), are well known to all physicians and they will be described briefly in turn with emphasis on their individual pathogenesis and evidence of hypo- or hyper- function of the pituitary and its surrounding neurologic structures.

A. *Fröhlich's Syndrome.*—This is a complex combination of findings—also known as dystrophia adiposo-genitalis—now held to be due to anterior lobe deficiency together with posterior lobe deficiency or a hypothalamic lesion (Table I). It was first described by *Babinski* in 1900, who should be given priority for the clarification of the syndrome.[9]

This condition, as its name suggests, is a syndrome in which obesity, sexual infantilism and dwarfism (if it occur during the growth period) are essential features.

TABLE I

LESIONS RESULTING FROM PITUITARY DYSFUNCTION

1. Anterior Lobe	Over Activity (Chromophile)	Acromegaly, Gigantism	Acidophile
		Cushing's Syndrome	Basophile
	Deficiency	Dwarfism	
		Simmonds' Disease	
		Acromicria	
2. Posterior Lobe Deficiency or Hypothalamic Lesion (or both)			Diabetes Insipidus
3. Anterior Lobe Deficiency together with Posterior Lobe Deficiency or Hypothalamic Lesion (as in Chromophobe Tumor or Rathke's Pouch Tumor)		*Dystrophia Adiposo-Genitalis* (*Fröhlich*)	a. Infantile or Juvenile Type b. Adolescent or Adult Type

(Modified from Best and Taylor)

Anterior lobe deficiency accounts for the sexual immaturity and dwarfing, whereas the obesity probably results from a lesion in the hypothalamus or the tuber cinereum. Fröhlich's syndrome is not due to a *specific* lesion as is acromegaly or gigantism (in which latter cases there is always present an acidophilic adenoma or a carcinoma derived from the anterior lobe) but it may result from pressure on the pituitary from a superimposed craniopharyngioma, from an endocrinologically inert chromophobe adenoma of the anterior lobe, or following injury or infectious disease.

over the pubis and axillae is sparse or absent, the skin of the face and body is smooth, soft and hairless; the hips are broad. In female subjects, the obesity is often extreme, a weight of 300 pounds being not unusual. In both sexes, the feet and hands are small and petite: the so-called "pretty hand". The basal metabolic rate is subnormal. Diabetes insipidus or narcolepsy are occasional accompaniments.

B. *Giants and Acromegalics.*—Giants and acromegalics occur from a specific lesion: adenomatous hyperplasia or carcinoma of the acidophilic cells of

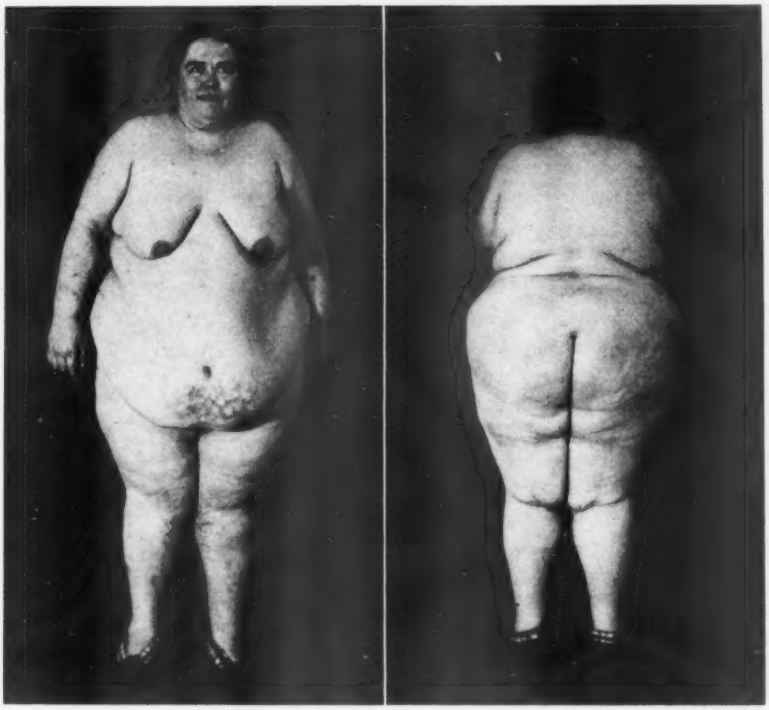

Fig. II.—(a) (b).—Twenty-seven years old; weight 350 lbs. Sella normal. Severe bitemporal headache; visual acuity normal. Note generalized obesity including extremities. Typical case of non-surgical adult Fröhlich's syndrome. (Obesity of Cushing's syndrome, on the other hand, is confined to the trunk and face, with sparing of the extremities; see Fig. IV.)

Fröhlich's syndrome appears in two forms depending on the age at which it develops: (1) the infantile or juvenile and (2) the adolescent or adult type (Fig. II). Polyuria, high sugar tolerance, somnolence, voracious appetite—especially for sweets—and stunted growth may occur. The fat boy of "The Pickwick Papers" was undoubtedly an example of this condition.

The male adolescent or adult type of Fröhlich's syndrome often appears effeminate in habitus. Hair

the anterior lobe (Table I). If the lesion occur in adolescence, gigantism supervenes; if it first develops during adult life, acromegaly is the result (Fig. III).

In Marie's first two acromegalic patients, amenorrhea was an early symptom which was ascribed to overwork and exposure to cold.

Headache—bi-temporal in location—is common and may be prostrating. Libido is increased at first but later declines. These patients succumb, if not to an intracranial extension of the tumor, to some

Fig. III.—Twenty-eight years old. Large sella, practically normal visual fields and acuity. Severe bi-temporal headache. Operated upon (elsewhere): Pituitary cyst demonstrated, followed by X-ray therapy with relief of headache. Note coarse features and large hands, typical of acromegaly.

cardiovascular complication associated with hypertrophic changes that affect the heart and blood vessels.

Whether or not neighborhood symptoms occur that demand surgical intervention depends upon the size attained by the tumor and whether it remains confined within its ballooned capsule or bursts through, pressing upon the optic chiasm and causing the typical bi-temporal hemianopsia and primary optic atrophy.

C. *Cushing's Syndrome.*—Cushing's syndrome is another example of hyperfunction of the anterior lobe (Table I) but, in this instance, of the basophile cells. In 1932 Cushing[10] first described a remarkable symptom complex due to a tiny growth (not gross enlargement) of the basophile cells. Since polyglandular symptoms are evident and since *hyperplasia* or even *tumor* of the *adrenal cortex* has been the more obvious lesion postmortem, that gland (the adrenal) has occasionally been indicted for the trouble and may indeed be greatly concerned with it.

The disorder is distinguished by a rapidly acquired plethoric and painful adiposity, confined to the face, neck and trunk. The arms and legs are thin but their surface is mottled and acrocyanosis is present. Purplish striae are present on the abdomen. In females, amenorrhea and hypertrichosis mark the establishment of the disease; the face becomes bearded. Polycythemia and vascular hypertension are decidedly common. The average duration of life is about five years. Hemianopsia and primary optic atrophy rarely occur as the gland is not grossly enlarged and the sella usually is normal or even quite small. We recently discharged such a patient with a right-sided hemiplegia following an apoplectic attack. She also had vascular hypertension and a small sella as well as marked hypertrichosis and amenorrhea together with enormous obesity of the trunk and quite thin extremities (Fig. IV). X-ray therapy is utilized for the control of the disease, although Pattison and Swan[11] report favorable results from implantation of radon seeds in the pituitary after failure of X-ray therapy.

D. *Chromophobe Tumors.* — Chromophobe tu-

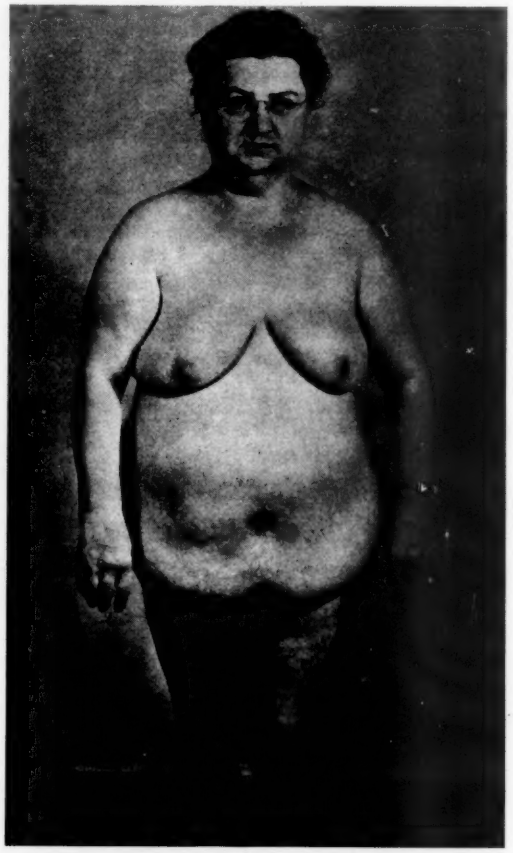

Fig. IV.—Forty-three-year-old woman with Cushing's syndrome. Note enormous obesity of trunk with relative sparing of lower extremities (compare with Fig. II—Fröhlich's syndrome). B. P. 210/140. Sella turcica and basal metabolism normal. This patient has weakness of right arm and leg from probable cerebral vascular accident. Definite hirsutes of chin. Severe headache greatly relieved by X-ray therapy of pituitary gland.

mors, on the other hand, although also derived from the anterior lobe, result in hypofunctional manifestations due to the crowding out, by the functionless mother chromophobe cells, of active basophile and acidophile cells, as well as impairing the function of the posterior lobe and the hypothalamus (Table I). These tumors are usually larger than the acidophile (acromegalic) type. Their larger size causes a greater likelihood of pressure upon neighboring structures and primary optic atrophy, bi-temporal or homonymous hemianopsia, bi-temporal headache, and a ballooned-out sella are the rule.

Constitutional signs of hypophyseal insufficiency in patients with chromophobe tumors are, to the trained observer, usually apparent. The adiposogenital syndrome of Fröhlich is occasionally but not always evident (Table I). There is a peculiar waxy pallor and smoothness of the skin, a tendency to put on weight and the males are obliged to shave only at infrequent intervals. Growth and sexual development may be impaired due to suppression of the secretions of the anterior lobe. Somnolence, obesity and diabetes insipidus, if present, point to diminution in function of the posterior lobe or the hypothalamus. The basal metabolic rate is characteristically lowered, whereas in the chromophile (acromegalic) type it is normal or elevated.

E. *Craniopharyngioma or Rathke's Pouch Cysts.*—These lesions arise from cellular rests in the neuro-buccal development of the pituitary body. Being congenital in origin, they commonly give symptoms early in life. Suprasellar calcification is seen in 80 per cent of the cases by X-ray examination. The growth may be solid or cystic and usually contains cholesterin crystals. It frequently produces the typical Fröhlich's syndrome (not always present) by compression, from above, of all the pituitary elements and surrounding nervous structures (Table I). Internal hydrocephalus occurs much more frequently than in ordinary pituitary adenomas as the tumor frequently encroaches upon the third ventricle. The constitutional symptoms closely resemble those of a chromophobe adenoma. Not all of the constitutional states, resulting from a craniopharyngioma, are alike. There may result a fat and fairly well-grown child, or a dwarf. These dwarfs and infantile children, so long as they escape general pressure symptoms, remain intellectually precocious, and may have a peculiarly appealing personality. It is only when hydrocephalus develops that life is threatened.

F. *Simmonds' Disease or Cachexia Hypophyseopriva.*—Simmonds' disease or cachexia hypophyseopriva is due to atrophy or destruction of the anterior lobe of the pituitary gland (Table I). The onset is insidious, usually in the third or fourth decade. The clinical picture is characterized by marked emaciation, precocious senescence, gastrointestinal upset, loss of secondary sex characteristics and extreme debility. In addition, hypothermia, bradycardia associated with vascular hypotension, a reduced basal metabolic rate and diminished salt and water excretion are present, with death usually terminating the well-developed syndrome. We have seen the Simmonds' syndrome develop postoperatively after subtotal removal of a chromophobe adenoma. This was not improved by administration of various anterior pituitary extracts. On the other hand, Horrax[12] has described marked relief of the Simmonds' syndrome *after* operation for chromophobe tumors.

In 1914 Simmonds of Hamburg[13] first described the syndrome. His patient, at the age of thirty-eight, had puerperal sepsis after the birth of her fifth child. During the next eight years she developed amenorrhea, muscular weakness, anemia, loss of weight and premature senility. She was hospitalized in coma and died without regaining consciousness. Autopsy showed generalized splanchnomicria with necrosis of the anterior lobe of the pituitary. Simmonds was the first to insist that the primary etiological factor, in his first case and in two others subsequently reported, was destruction of the anterior pituitary lobe.

Calder[14] in 1932, analyzed seventy cases of Simmonds' disease in the literature and found that in most cases the basal metabolic rate was subnormal and the blood pressure invariably was low. In females, menstruation ceased and sterility ensued. Without exception, autopsy revealed destruction of the anterior lobe of the pituitary gland. An interesting feature of the condition is that many of the symptoms resemble *Addison's syndrome,* the chief differentiation being the pigmentation of the skin generally present in the latter disease. Autopsy in Simmonds' disease usually shows at least adrenal cortical hypoplasia, if not necrosis, as a result of the generalized splanchnomicria and therefore the asthenia, low blood pressure and subnormal tem-

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perature of Simmonds' disease may well be due *entirely* to secondary involvement of the adrenal cortex.

Anorexia nervosa must always be rigidly excluded in every case of Simmonds' disease.

G. *Mixed Types.*—Occasionally curious *mixed* syndromes of pituitary dysfunction are seen, especially in the adenomas, combining certain features of the Fröhlich syndrome and of acromegaly, pointing to an undoubted concomitant involvement of the chromophobe and the acidophilic cells of the anterior lobe.

H. *Diabetes Insipidus.*—The most outstanding condition which is presumably associated with hypofunction of the posterior lobe is diabetes insipidus but this may also be a manifestation of hypothalamic dysfunction alone (Table I). Cushing[3] has given the clearest account of this problem so far available. Most of the earlier experimental hypophysectomies on dogs now unquestionably lie open to the just criticism that a coincidental damage of the floor of the third ventricle also occurred. Cushing summed up our present knowledge of the causation of diabetes insipidus as follows: "The evidence at hand seems reasonably convincing that the disorder cannot be attributed to any single specific lesion. Experimental injury of the diencephalon appears to give the most pronounced and enduring polyuria, yet posterior lobe injury in the rat in the absence of diencephalic involvement will produce a definite, although less striking, diuresis."

Diabetes insipidus occasionally accompanies tumors of the pituitary gland and of the hypothalamic region. It has been shown by Bremer and Bailey[15] that in animals, puncture of the floor of the *third* ventricle alone will produce *diabetes insipidus* just as Claude Bernard's classic puncture of the floor of the *fourth* ventricle caused a glycosuria, the so-called "medullary" *diabetes mellitus.*

Best and Taylor[16] concur in Cushing's statement that it is probably correct to look upon diabetes insipidus as the result of a disorder affecting the integrity of the posterior hypophyseal—hypothalamic mechanism—rather than as being dependent specifically upon either the posterior pituitary or the hypothalamus alone.*

*Dr. Carlos Gama (University of Sao Paulo, Brazil) has recently greatly reduced a severe polyuria in a patient with diabetes inspidus by transplanting a steer's hypophysis into the thigh of his patient. He advocates preparing patient and donor with each other's serum *before* the transplant: "Transplante de Hypophyse bovina Ao Homem," Sao Paulo, 1939.

I. *Pituitary Dwarfs and the Lorain Syndrome.*—The arrested skeletal development which results from deficiency of the growth hormone of the anterior pituitary is spoken of as the *Lorain type of infantilism.* These dwarfs are usually, though not invariably, undeveloped sexually. They do not show deformity or, as a rule, mental inferiority, and are generally not unattractive in appearance (Fig. V). Sometimes, however, except for their miniature stature, they appear older than their years (progeria). Treatment with the growth hormone of the anterior pituitary must be begun before the epiphyses have united in order to be effective, according to Sevringhaus.[17]

Fig. V.—Three years old. Normal sella. Normal intelligence. Height: 76 cm. (should be 94 cm.). Head: 47.5 cm. in circumference (should be 50 cm.). Weight: 22 lbs. (should be 32 lbs.). A sibling, aged 4, normal. Typical pituitary dwarf; treated with antuitrin-G hormone.

J. *Laurence-Biedl-Moon Syndrome.*—To complete the syndrome of hypofunctional pituitary states, mention must be made of the *Laurence-Biedl-Moon Syndrome.* This condition, hitherto ascribed to generalized pituitary deficiency (of both lobes), is now believed to be due to involvement of the hypothalamus alone. The chief features of the disease are: obesity, sexual infantilism, retinitis pigmentosa,

polydactylism or syndactylism, mental deficiency and a familial tendency associated with occasional consanguinity.

K. *Miscellaneous Conditions.*—Carcinoma may occur in the pituitary gland and also in craniopharyngiomata. Usually the diagnosis is made only on histological examination which demands more intensive post-operative X-ray treatment than otherwise would be the case. Gumma, tuberculoma and diffuse tuberculosis of the pituitary gland all have been noted by various observers. Diffuse tuberculosis confined to the pituitary gland has been noted only once to our knowledge. This was in a case operated on by Dr. C. C. Coleman at the Medical College of Virginia in 1936; this patient was free of other evidences of tuberculosis and clinically resembled a case of chromophobe adenoma. The pituitary tissue, when examined by Dr. A. C. Broders, of the Mayo Clinic, showed diffuse tuberculosis of the pituitary gland. Inquiry[18] at most of the Neuro-Surgical Clinics of this country and Canada disclosed no similar lesion on record. The patient made an uneventful recovery, bi-temporal hemianopsia disappeared and she is still alive and well to date with no signs of recurrence three years after operation. Removal of tuberculous lesions from the intracranial cavity, whether in the pituitary region or in the posterior fossa, is often followed by tuberculous meningitis.

2. *Remarks on the Therapy (Other Than Hormonal) of Certain of the Previously Described Lesions in Part II:* It is generally agreed that the only effective therapy in cases of adenoma or carcinoma of the pituitary gland is either surgery, roentgen therapy or both. Practically all observers agree that X-ray treatment is more effective in the chromophile (acromegalic or gigantic) types than in the chromophobe (Fröhlich types) although this is not always true, as demonstrated by a case of chromophile tumor operated on at the Lahey Clinic by Dr. Gilbert Horrax several years ago which had received intensive X-ray treatment elsewhere with little improvement in vision, although the tumor was not cystic; operation greatly improved the visual defects.[19] *The neuro-surgical concensus of opinion concerning treatment of pituitary tumors in general is that surgery is indicated only if there is definite or severe visual impairment, when the patient is first seen or if there are severe intractable headaches without visual impairment that are not adequately relieved by X-ray therapy.* If the patient is first seen with an enlarged sella and a well marked primary optic atrophy in one or both eyes together with partial blindness in one or both eyes and (or) a more or less well developed hemianopsia, neurosurgeons believe that immediate operation is indicated *without resort to preliminary X-ray treatment,** especially if the lesion be of the more common chromophobe (Fröhlich) type, which is known to be less susceptible to X-ray therapy. It is only fair to state, however, that roentgenologists are inclined to recommend preliminary X-ray treatment in all patients with an enlarged sella and visual failure with or without headache. If *this* be done, the patient should be hospitalized with frequent careful observations of the visual fields and acuity, as, occasionally, X-ray treatment, in producing an initial edema of the gland, may *impair* vision still further. In Cushing's clinic, one such gland expanded after X-ray treatment to the extent of breaking through the floor of the sella into the sphenoid sinus, preceded by great reduction in vision.

The operative mortality in cases of pituitary tumor in competent hands should not exceed 5 per cent. Needless to state, all such lesions should be irradiated post-operatively. Henderson[20] found, in Cushing's series, that in the *chromophobe* group 57.5 per cent of the patients, with transfrontal operation only, remained free from recurrence for five years, whereas 87.1 per cent were relieved for five years or more if X-ray therapy were given post-operatively. No similar statistics for a comparable number of *chromophile* tumors are available to the writer's knowledge.

It must be said, however, that the efficacy of X-ray therapy, in the last eight or ten years, has been considerably enhanced compared with the methods utilized in most of Cushing's cases, and this fact should be borne in mind in determining the form of therapy in any individual case. One well-founded objection to pre-operative irradiation is that it is subjecting a *presumed* tumor to a destructive agent without histologic verification—certainly the only intracranial surgical lesion so treated. However, all observers agree that, unless there is definite visual impair-

*Since this paper was first written, Dr. Francis Grant has advocated preliminary X-ray therapy for *all* pituitary tumors with severe headache, *even if vision be seriously impaired.* Dr. Ernest Sachs took exception to this statement, believing that *surgery* is always indicated as a *primary* procedure in these cases, when vision is seriously impaired. *J. A. M. A.*, 113:1279-84, September 30, 1939.

ment, irradiation of the pituitary region is certainly indicated if there is an enlarged sella turcica and severe headache on the assumption that a tumor is present. Certain pituitary lesions are relieved by roentgen therapy, as in Cushing's syndrome; others, such as *adolescent* pituitary dwarfs, by hormonal therapy; still others, such as adult dwarfs and most cases of Simmonds' disease, are not effectively relieved by any known therapeutic agent—in the present state of our knowledge. Endocrine symptoms alone are never to be considered as sufficient justification for surgery even in the presence of an enlarged sella; only definite visual impairment or severe headache not relieved by X-ray therapy are, at this time, considered adequate indications for operation.

Surgery is the only effective agent in the management of craniopharyngiomata as they are usually cystic and indifferently affected by roentgen therapy. Cushing has rightly emphasized, however, that even a partial extirpation of this lesion is one of the most hazardous operations in neurological surgery. In contrast to intra-sellar growths, the mortality is high. The chief reasons for this are two: (1) in the process of removal, unavoidable damage may be done to the floor of the third ventricle (which adjoins the top of the tumor) with only too frequent hyperthermia and (or) hypersomnia and death; (2) increased intracranial pressure is frequently present in these tumors, as contrasted with the primary intrasellar adenomas, thus greatly increasing the hazards of the operation, especially as it is a basilar tumor. The almost unanimous opinion at the present time is that these lesions are best treated by multiple tappings of the cholesterinized fluid through one or two anterior burr openings with subsequent X-ray treatments in the hope of destroying the secreting cells. Patients can frequently be carried along by this method for an indefinite period.

PART III. PITUITARY ORGANOTHERAPY

(1) *Anterior lobe* preparations are of only limited success:

(a) The growth hormone, known commercially as antuitrin G, produces beneficial results in adolescent dwarfs during the growth period, but *adult* pituitary dwarfs are not sufficiently stimulated; a more potent extract is needed.

(b) The sex or gonadotropic hormone of the anterior lobe, known commercially as antuitrin S, is of no value in sex maturing a hypogonadal individual. Following the discovery of prolan A and B (anterior pituitary-like hormone) in pregnancy urine, preparations from such urine have been used in the treatment of conditions supposedly the result of deficiency in the gonadotropic hormone. For example, it is undoubtedly beneficial in certain cases of functional uterine bleeding and remarkable results have been obtained in some cases of undescended testicle *not* due to a mechanical defect. However, the sex hormone of the anterior lobe is of little or no value in endocrinopathic amenorrhea.

In *Simmonds' disease* most observers have obtained little improvement with anterior pituitary extracts which are apparently indicated as replacement therapy.

(c) *Effect of Antuitrin on Myasthenia Gravis.*—The only other condition in which anterior pituitary extracts have proved of benefit is, curiously enough, myasthenia gravis. Following the favorable report of Simon[21(a)] in 1935, we administered *antuitrin* hypodermically (this substance being an acid-aqueous extract of the anterior lobe) in a case of typical myasthenia gravis with gratifying results so that the patient has now returned to his full activity as a minister, having required no antuitrin or other therapy for more than two years.[21(b)] This patient responded only slightly to prostigmine therapy.

It is known that Simmonds' disease, pathologically characterized by invariable atrophy of the anterior pituitary, has as its most outstanding symptom *profound muscular weakness.* It is at least reasonable to assume, in certain favorable cases of myasthenia gravis (also, like Simmonds' disease, characterized by profound muscular weakness and also possibly related to anterior pituitary hypofunction) that antuitrin will restore the patient to improved muscular activity by supplying the absent or diminished hormone of the anterior pituitary lobe.

(2) *Posterior lobe* preparations, although apparently not glandular in origin—unless one accept the belief that the hyaline bodies in the posterior lobe are derived from the *glandular* pars intermedia and also that these hyaline bodies have secretory properties—are on the whole, more powerful physiologically and pharmacologically than are the anterior lobe preparations.

A. *Pituitrin,* which is the group name for all posterior lobe hormones combined, produces definite changes in the cardiovascular and urinary systems

and profoundly affects smooth muscle contraction and metabolism.

(1) and (2). *Oxytocin and Pitressin*—both derived from pituitrin, the active posterior lobe hormone—overlap somewhat in physiological effect. Oxytocin, known commercially as pitocin, is used to some extent by obstetricians to cause uterine contractions before and during delivery, to aid in the expulsion of the fetus or placenta and to combat post-partum uterine hemorrhage.

Pituitrin and pitressin, which latter drug is also known *commercially* as pitressin, have a limited effect in stimulating bowel action and allaying abdominal distention.

Pituitrin raises the blood sugar by antagonizing insulin and therefore hypophysectomy should lower the blood sugar. It is known that removal of the pituitary gland in a dog with hyperglycemia (as a result of previous partial pancreatectomy) causes a dramatic fall in blood sugar. One is led to speculate as to whether, sometime in the future, an accepted treatment for diabetes mellitus will be a partial hypophysectomy (accomplished surgically or by X-ray therapy).

Pituitrin has anti-diuretic properties in pathological individuals and is used in the treatment of diabetes insipidus but its action usually is transitory. Nasal sprays and snuff are utilized for this purpose. It has no effect when the diabetes insipidus is due to hypothalamic disease alone.

It has been aptly stated by the pharmacologist Sollmann[22] that it is remarkable, in regard to the pituitary as in the suprarenal glands, that those portions of these two glands which are most important to life (suprarenal cortex and the anterior pituitary) have the *least acute* pharmacologic effects. The suprarenal medulla and the posterior pituitary, from which are derived powerful pharmacologic substances, appear to be of relatively minor importance to the existence of the organism.

The recent publication by Crockett[23] and the comment by Main[24] are of great value in clarifying our views on the endocrine preparations now available to the profession. A central official clearing house for the standardizing of these preparations is certainly greatly needed as the present methods of assay of the various pharmaceutical houses differ widely.

Conclusions: (In reference to pituitary glandular therapy): The pituitary lags far behind the outstanding success that has been obtained with thyroid extract in cretinism, with insulin in diabetes mellitus and with parathyroid hormone in hypoparathyroid states. With regard to the pituitary, there have been no definite *consistent* therapeutic results in the treatment of pituitary glandular deficiencies by means of pituitary extracts, or, indeed, by any known therapeutic agent.

The value of any pituitary preparation in the treatment of any pituitary deficiency is questionable except in (1) certain cases of *diabetes insipidus,* (2) *myasthenia gravis* (possibly an anterior pituitary deficiency disease in part), (3) *adolescent pituitary dwarfs* who are not under 50 per cent of their normal growth increment and whose epiphyses have not yet united when first treated, (4) certain cases of undescended testicle not due to a mechanical defect, (5) an occasional case of Simmonds' disease, (6) certain cases of functional uterine hemorrhage. In these six conditions, good results have been obtained. Oral administration of pituitary preparations (in the treatment of diseases characterized by pituitary deficiency) is generally held to be useless and oral administration, in fact, of all endocrine products, has been effective only in the case of the thyroid gland (cretins), and the adrenal cortical hormone. Then again, the cost of repeated *injections* is almost prohibitive for many patients.

The development of glandular therapy is rather hindered by premature enthusiasm which is inclined to dispense with adequate controls and often with critical diagnosis. This undue enthusiasm may interpret psychic manifestations as scientific effects of the extracts administered and it may depend more on credulity based on expected results rather than on facts (Sollmann).[22]

Some day, aided by further investigation and development of pituitary extracts, perfection of these preparations as effective agents in combating the devastating effects of pituitary deficiency disease will doubtless be attained.

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MEDICAL ASPECTS OF ACUTE PYELITIS.*

NATHAN BLOOM, M.D.,
Richmond, Virginia.

Acute pyelitis was first recognized and described by Rayer[1] in 1837. Inflammation in the pelvis of the kidney, with its resulting clinical syndrome, is a very common malady but unfortunately very little pathological material is available to confirm our clinical impression of a disease entity. The anatomical structure of the genito-urinary system prevents the development of just a simple pyelitis. The adjacent ureters or kidneys invariably must be involved in the inflammatory reaction. However, from a clinical standpoint there are certain cases in which inflammation of the kidney pelvis is a dominating factor.

There must be bacterial invasion of the genito-urinary structures to produce acute pyelitis. The organisms commonly found in this disease are the colon bacillus, staphylococci, streptococci, and tubercle bacilli. The finding of colon bacilli in the urine is so frequent that some observers consider this organism part of the normal flora, but under aseptic precautions and without parenteral infection, normal urine should be sterile.

The development of a pyelitis usually depends on a ureteral obstruction followed by urinary stasis. The bacterial organisms then reach this area of the genito-urinary tract by ascending from the bladder through the ureteral lymphatics or invade the blood stream and then are carried through the kidneys, localizing in the pelves. Occasionally the spread of infection is through the ureteral lumen. This has been noted in tuberculous infections of the kidneys, in which the spread is from the kidneys to the blad-

*Read at a meeting of the staff of the Retreat for the Sick Hospital on March 20, 1939.

der and then ascends through the ureteral lumen to the opposite kidney.

Acute pyelitis is not confined to any special group of individuals. It may occur in the infant or the adult and at times produces very unusual symptoms that confuse the diagnosis. A typical case begins with chills, high fever, pain in the costo-vertebral angles, the loins, or the lower quadrants of the abdomen. The urine invariably contains much pus, bacteria, albumin, and at times red blood cells. Frequency of urination with tenesmus is not uncommon. None of these clinical phenomena in themselves are characteristic of pyelitis, but the combination of chills, fever, and pyuria, leads us to the consideration of this malady.

There are many other acute infectious abdominal conditions which may simulate acute pyelitis. Acute appendicitis will very frequently be associated with chills, fever, and loin pain. Pyuria may be present if the appendix is in close proximity with the ureter; this is not unusual in the retro-cecal type of appendix. Acute cholecystitis may begin with chills, fever, and abdominal pain, but the pain radiation is posterior and upwards towards the right scapula. Jaundice is usually present and pyuria should be absent. In children early lobar pneumonia will begin with abdominal pain and not infrequently the urine may contain pus. A careful chest examination should reveal the underlying pathology. Abdominal pain with chills and fever may occur in liver abscess. The pain is usually more anterior and higher in the abdomen than in pyelitis. Jaundice may be present but pyuria should be absent. Sub-diaphragmatic abscess is frequently confused with acute pyelitis; a distinguishing feature in this condition is shoulder top pain. Peri-renal abscess may develop all of the phenomena we find in pyelitis but usually the pain is well localized over the affected kidney and at times definite fluctuation may be demonstrated in this area.

When confronted with a suspected case of acute pyelitis an attempt should be made to determine the causative organism. Obviously the finding of tubercle bacilli in the urine tends toward a more serious prognosis than if the condition were due to a B. coli or staphylococcus infection. It is also necessary to determine the degree of functional impairment to the kidneys. If there is an acute obstruction to both ureters the case may present a picture of uremia. Fortunately this is an infrequent occurrence but severe renal impairment is possible and an attempt should be made to determine the degree of renal insufficiency.

There are many simple kidney function tests. The phenolsulphonephthalein test is based on the ability of the kidneys to excrete this dye. The test has no value in the presence of large amounts of gross blood. After intravenous injection of the dye, the urine is collected at the end of fifteen, thirty, sixty, and 120 minutes. At least 25 per cent of the dye should be excreted within thirty minutes in normal individuals. A marked decrease in the amount of dye excreted means either obstruction or severe renal damage. The non-protein nitrogen of the blood should also be determined; usually in acute pyelitis if dehydration is not too severe, the non-protein nitrogen should remain within normal limits. One of the most important kidney function tests is the concentration test. It is based on the fact that normal kidneys will vary in their excretory ability during twenty-four hours. The method is to allow the patient fluids up to 6 P. M. during the day, collecting the urine at two-hour intervals. No fluids are allowed after 6 P. M. and all of the urine from that time until the following morning is collected as one specimen. Normally the night urine should be less than the day urine and its specific gravity should be above 1.018. The finding of an increase in nocturnal urine output above 500 cc., with a low maximal specific gravity of 1.016 or less, means severe kidney damage. A fixation of the specific gravity with less than two to four points difference in specimens and a range below 1.016 also signifies severe impairment in kidney function. If after performing these various procedures it is noted that there is evidence of kidney damage, it might be unwise to carry out any instrumental procedures except with extreme caution.

Genito-urinary complications are usually the rule rather than the exception in acute pyelitis. It is not unusual to have ureteral stricture, renal calculi, tumors, or congenital anomalies, associated with the inflammatory process. Much interest has recently been placed on hypertension as a complication in renal infections. The possibility of an association between kidney infections and hypertension had not been considered until the recent work of Goldblatt[2] on the production of hypertension in dogs. This definitely revived the idea that in some cases hypertension affecting human beings might be caused pri-

marily by renal infection, particularly if the arterial supply to the kidneys was damaged. Longcope[3] recently discussed the relationship between chronic bilateral pyelonephritis and hypertension. He found that definite hypertension occurred in 50 per cent of twenty-two cases of pyelonephritis. Butler[4] reported on a series of six children who had chronic pyelonephritis associated with hypertension and in two of these cases in which the pyelonephritis was unilateral, nephrectomy was performed and the blood pressure returned to normal. Barker[5] recently reported a case of unilateral, chronic, atrophic pyelonephritis in an adult; the hypertension developed after the chronic pyelonephritis and the patient's blood pressure returned to normal following the removal of the infected kidney. This does not mean that hypertension is a frequent complication of acute pyelitis but the possibility of sufficient renal damage with later development of hypertension should not be overlooked.

It is believed that most of the cases of acute pyelitis usually subside very promptly after routine treatment, but we should always be on the alert for the various complications that may occur, changing a very simple malady into a very serious and sometimes fatal disease.

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1006 West Franklin Street.

THE TREATMENT OF PYELITIS.

CHARLES M. NELSON, M.D.,
Richmond, Virginia.

Pyelitis, for the purpose of this discussion, may be arbitrarily divided into two types, simple and complicated. By simple pyelitis I mean, and I think this is the usual concept, a superficial acute inflammation involving the mucosa of the renal pelvis, the tip of the renal papilla and a varying proportion of the lower urinary tract. By complicated pyelitis I mean that there is either some pre-existing condition in the urinary tract which exaggerates and prolongs the disease, or the disease spreads from its initial site at the tip of the papilla up along the lymphatics and blood vessels of the kidney to involve in an acute process all of the interstitial renal elements, to eventuate usually in the production of multiple abcesses throughout the kidney substance—the so-called pyelonephritis.

The primary regard in the treatment of simple pyelitis must be for the comfort of the patient, and for this reason therapy must be at first directed toward the relief of the bladder symptoms which are so frequently the low companions of the more highly placed infection. To this effect, alkalinization by means of sodium bicarbonate and fruit juices together with a mixture of tinctures of belladonna, hyoscyamus and opium are of value. In the female, daily bladder irrigations with boric acid or some similar mild solution serve the purpose of cleansing the bladder and of allowing one to determine the presence or absence of residual urine. Residual urine in the female bladder, particularly following pelvic operations or parturition,[1] is more common than generally supposed and will act as a reservoir of infection. After irrigation an ounce of 10 per cent neo-silvol, 1 per cent aqueous mercurochrome, ¼ per cent protargol or some similar preparation may be left in the bladder. If frequency and burning are extreme, one ounce of benzocaine 4 per cent in olive oil,[2] a fairly powerful anesthetic, may be instilled instead of the antiseptic solution. During the acute stage of the disease either water by mouth, or normal saline, or a 5 per cent solution of glucose parenterally is more to be desired than drugs. The fluid intake at this time should probably not be less than 5,000 c.c., and the output, certainly after the

second day of treatment, should be correspondingly high.

The administration of drugs at the present time is predicated on a knowledge of the infecting organism. We have at our disposal at least three effective drugs for this purpose—sulfanilamide, mandelic acid and neo-arsphenamine—each of which has a definite place in the therapy of the disease, that place depending on the bacterial agent. Mandelic acid is of little value in infections caused by organisms other than the colon group and streptococcus fecalis. Sulfanilamide has its greatest use in coccal infections and those due to the proteus group, although it will attack E. coli, while neo-salvarsan is rarely used in other than the staphylococcus infections. It is a simple matter to determine the type of organism—a carefully stained smear of the sediment from a centrifuged catheterized specimen will usually enable one to determine its morphology, although definite identification may require repeated cultures which, as we all know, is a time consuming procedure. Fortunately, in the majority of cases the morphology of the organism, whether it is a bacillus, or staphylo- or streptococcus is all that need be known to initiate treatment.

For the patient with uncomplicated pyelitis, then, we can plan a regime somewhat similar to the following:

1. Restoration of fluid balance.
2. Treatment of bladder symptoms.
3. Drug therapy.

a. If the organism is a bacillary form the patient should be given ammonium chloride in sufficient dosage to produce a urinary pH of 5.2 or less which is usually accomplished by the administration of fifteen grains t.i.d. After the pH is 5.2 or less, mandelic acid is given in doses of 180 to 200 grains a day divided into four daily doses. We usually prescribe one-half ounce of the elixir of mandechlor four times a day as being the least expensive of the various preparations available. In a series of cases recently studied at the Medical College of Virginia[3] this regime proved entirely satisfactory in the colon bacillus group.

b. If the organism present is a coccus, especially a streptococcus, or if it splits urea as determined by an alkaline reaction and the odor of the urine, we usually prescribe sulfanilamide in fifteen-grain doses four times daily for three days. If, by that time, the urine has not markedly improved we are of the opinion there is little to be gained by continuing the drug, since in all probability the organism present is sulfanilamide resistant. Of the two drugs, the latter is definitely more valuable, not only because it attacks more types of organisms, but also because there is not the same necessity for limiting fluids and acidifying the urine, both of which procedures are not without danger during the acute phase of the disease.

c. If the organism present is a staphylococcus, neo-arsphenamine is said to be the drug of highest therapeutic efficiency. Most urologists have seen the apparent complete abortion of an acute pyelitis following administration of the drug and have seen this effect often enough to be convinced of its value as a therapeutic agent. It is impossible to see a very ill patient running a septic temperature receive a drug and never thereafter during hospitalization run any fever without being of the opinion that the drug was of some benefit. Of course, this hoped-for result is all too rarely the case, but it occurs sufficiently often to make it worth while to give the drug a trial. Like sulfanilamide it can be administered during the acute stage. It may be repeated as often as every other day for three doses.

The other drugs, caprokol, hexamethylenamin, serenium, pyridium, *et cetera*, can not compare in therapeutic potency with any of the three above mentioned and are not at the present time indicated in the treatment of this disease.

From these brief remarks it can be seen that there is no special knowledge nor is there any special procedure required in the treatment of simple pyelitis. Once assured of the diagnosis, the treatment is entirely medical. Certain of these cases, however, and, it must be confessed, a fairly large percentage, fail to improve as rapidly as could be desired; others, while symptomatically improved, persist in showing pus and occasionally a few red blood cells in the urine. A third group, apparently free of any infection on discharge, show frequent recurrences or exacerbations. All three of these groups require further study and usually other methods of treatment than those outlined above.

The first group—those who run a septic temperature more than five to six days after onset of symptoms—exercise the ingenuity of the physician more than any other type of case. There are usually two possible explanations for this therapeutic failure, the first being that there is inadequate drainage of

the kidney from whatever cause—stone, stricture, bladder neck obstruction—or the disease has spread throughout the renal parenchyma with the production of an acute pyelonephritis. With the latter complication the patient is dangerously ill and its presence or absence should be determined at as early a date as possible. The means of determining this are: First, rule out a residual urine by passing a ureteral catheter to the pelvis of the kidney and finding out whether or not it is empty. If retained urine is found the catheter should be left in place and the pelvis kept as empty as possible, no other procedure being carried out until the patient's temperature has subsided. If, however, there is no residual urine in the kidney pelvis and it is observed that the disease is progressing as evidenced usually by the septic temperature, a rapidly falling hemoglobin and a decrease in the patient's P. S. P. output, we are faced by the most difficult problem in urological surgery. Drug therapy, especially sulfanilamide, should be pushed, and 0.3 gram of neo-salvarsan may be given while the sulfanilamide is being administered. These patients invariably show a marked decrease in their renal output and almost invariably a severe acidosis. The CO_2 combining power should be checked frequently and alkalies administered, as indicated, either by mouth in the form of sodium bicarbonate or parenterally in the form of sodium lactate.[4] If there is still no improvement and the patient's condition remains critical, recourse may be had to the intravenous administration of mercurochrome 1 per cent in aqueous solution.[5] This drug has fallen into disrepute because of the large doses originally given which produced violent reactions—amounting in some cases to death. Nevertheless, it has been shown and I myself have seen that, with this type of infection, the drug is a therapeutic agent second to none and I should not hesitate to use it in cases in which other measures are obviously failing to avert a lethal exit. The dosage at present is based on the body weight of the patient.[6] A convenient rule-of-thumb in arriving at the dose is to divide the weight of the patient in pounds by the constant figure 8.8. The quotient obtained represents the number of c.c. of 1 per cent solution required to deliver 2.5 mgm. per kilo of body weight.

The second group—those patients who improve symptomatically, but whose urine fails to clear up—should have the advantage of a thorough urological examination. The source of this persistent pus and blood should be determined and appropriate treatment instituted. The commonest cause of this persistence is inadequate drainage somewhere along the course of the urinary tract—bladder residual, stricture or stone in the ureter, or aberrant renal vessels, causing residual in the renal pelvis. The examination should include cystoscopy and pyelography. This procedure is preferable to intravenous urography since the majority of these patients require cystoscopic treatment of some kind and diagnosis and treatment can be combined in the one procedure. Treatment, of course, is aimed at the relief of obstruction, either by dilatation of the ureter or removal of calculi present. The possibility of stricture of the female urethra should not be overlooked. Foci of infection should be eliminated.

The third group—those prone to frequent exacerbations—also should have a careful cystoscopic and X-ray examination. In addition to this, a very thorough search for foci of infection should be instituted. Tonsils, teeth, sinuses, and the cervix should be examined carefully and, if infected, treated vigorously.

In closing, there is one point I should like to emphasize: Whatever the treatment necessary for these patients, they should be followed until the urine becomes and remains free of infection. The time to effect a cure of pyelitis is at the time of the first attack. Every means should be exhausted before condemning the patient to a life of persistent infection with its frequent flare-ups and increased incidence of stone formation.

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Professional Building.

INCIDENCE OF CERVICAL PAIN ASSOCIATED WITH RENAL OR URETERAL CALCULI.

SAMUEL D. FAILLA, M.D.,
Assistant Resident Surgeon,
and
GEORGE A. WATSON, M.D.,
Rotating Interne,
Watts Hospital,
Durham, North Carolina.

It has been observed by us that cervical pain was associated with renal or ureteral calculi. In these cases no further signs or symptoms about the head or neck have been elicited either by history or physical examination. Therefore, this clinical entity apparently was not confused by the addition of other complaints.

The purpose of this paper is to discuss this cervical pain syndrome which has been in some cases of such severity that the original complaint of renal or ureteral calculus was almost completely overshadowed. Although this clinical picture may be well known, we offer this emphasis because of its evident absence in medical literature and its apparent neglect in medical teaching.

Our recent experience is the more pointed because the consecutive cases presenting this picture were of such severity that we believed it necessary to look back on past case records to see whether it had been obtained in either the history or elicited in the physical findings or stated in the progress of the patients. In this we were unsuccessful. Consequently, we are of the opinion that it merits an attempt to clarify this intriguing diagnostic problem. This is further narrowed in that pyelitis or pyelonephritis, although presenting pain in the kidney areas, is not accompanied in any of our cases by cervical pain. The problem then resolves itself definitely to a discussion of neurological anatomy and physiology of the kidneys and ureters.

The sympathetic system is widely distributed over the body, especially in the head and neck and in the thoracic and abdominal cavities. The sympathetic trunks are two nerve cords which extend vertically through the neck, thorax, and abdomen, one on each side of the vertebral column. In the abdomen the sympathetic trunk gives off branches which enter into the formation of nerve plexuses. These lie in front of the aorta and surround the origins of the larger arteries to the alimentary canal. We are mainly interested in the aorticorenal ganglia.

The lateral ganglia of the sympathetic chain are connected with all the spinal nerves, just after they have given off their posterior divisions, by means of the rami communicantes which are of two kinds, white and grey. The white rami are formed by fibers which have their origin in the spinal cord; whereas, the grey rami represent fibers which, arising in the sympathetic ganglia, run back to join the spinal nerves. The visceral outflow represented by the white rami is limited to a distinct region of the cord, viz., from the first thoracic to the third or fourth lumbar nerve roots; whereas, the grey rami pass from the sympathetic to all spinal nerve roots.

As we are dealing primarily with the kidneys and ureters, we are interested in the subdivision of the sympathetic system known as the aorticorenal ganglia. Pain cannot be produced by pinching or cutting the thoracic viscera. Acute visceral pain is caused by disease as in a renal calculus or in the passage of such along the ureter. The attempt to pass a renal calculus or the passage of this calculus down the respective ureter initiates visceral reflexes which are conducted to the sympathetic trunks by the grey rami, and thence cephalad to the cervical ganglia, thus producing the clinical picture of cervical pain. An additional physiological factor is now introduced. This stimulation of the sympathetic system results in an increased outflow of adrenalin which is sympathicomimetic in its action and serves to augment the pre-existing physiological condition.

Fifteen consecutive cases with positive roentgenogram findings of renal or ureteral calculi have come under our observation. Fourteen or 93 per cent, of these simultaneously complained of either pain in the kidney region or pain radiating down to the groin, along with severe cervical pain. At first this complaint seemed incongruous with the positive X-ray findings. The usual remedies such as acetylsalicylic

acid and the removal of the pillow failed to alleviate the existing condition. Morphine and atropine sulphate temporarily rendered them free of both renal, ureteral, and neck pain. As soon as the effect of the drugs became lessened, the original complaints were registered again. Complete relief of renal or ureteral pain was in all cases associated with the disappearance of cervical pain.

Although this series is quite small, the high percentage of positive cervical pain complaints justifies what we believe to be an important factor in the symptomatology of renal or ureteral calculi.

THE FEMALE CLIMACTERIC.*

E. C. HAMBLEN, M.D.,
Durham, North Carolina.

The natural span of life is characterized by three main phases; a period of growth and development, one of florescence and maturity, and one of old age. The climacteric, of which the menopause or cessation of menstruation is but an isolated event, represents a transition characterized by the loss of the power of propagation, by a decline in the sexual functions and a regression of the sexual organs, and by the beginning of somatic senility. The climateric woman is not necessarily an old woman, but a mature woman who has begun to age. It seems unnecessary to state that the climacteric is a physiological phase of the process of aging, yet much that has been written in recent years upon this subject may lead one to regard this process as fundamentally a pathological one. If this be true, then, as Richter has noted, life itself has indeed become a disease.

Cause: The fundamental cause of the climacteric is the development of a refractivity of the ovaries to regulatory influences of the pituitary. A delicately coordinated integration of function of ovaries and of pituitary characterizes the gynecic physiology of maturity. The anterior lobe of the pituitary exerts certain gonadotropic influences which are manifest fundamentally by stimulation of the graafian follicles, the induction of ovulation and the formation and persistence of corpora lutea. These characteristic cyclic phenomena of the ovaries are attended by quantitative and qualitative alterations in secretory activity. Two ovarian hormones, one of which possesses estrogenic properties and the other of which produces progestational changes are well known chemically and pharmacologically. Fluctuations in the concentrations of these hormones in the tissues and fluids of the body condition or regulate the gonadotropic function of the pituitary. The synergistic and antagonistic relationships between the two ovarian hormones and the two gonadotropic influences of the pituitary constitute the labile, dynamic, and ever changing hormonal system of the menstrual cycle.

Watson, Smith and Kurzrok[1] have supplied clinical proof that the ovaries of climacteric women are refractive to the gonadotropic influences of the pituitary. They have observed that injections of gonadotropic extracts prepared from the serum of the pregnant mares (containing gonadotropes similar to, if not identical with, those of the pituitary) were followed by the formation of multiple cysts in the ovaries of women during the third decade of life, but they failed to observe similar responses in the ovaries of women in the fourth decade or older. At times they observed a unilateral refractivity, one ovary responding and the other ovary showing no alteration.

It seems logical to assume then that beginning senility of the ovaries results in a failure to carry on their normal gametokinetic and endocrine functions because of an inability to respond adequately to the gonadotropic influences. The first grade of ovarian failure is characterized by the non-occurrence of ovulation and the loss, as a result, of the progestational phase of the cycle. Post-ovulational corpora lutea cease to occur and the elaboration of progesterone ceases. The ovarian cycle, therefore, becomes uniphasic rather than biphasic. Estrogens may continue to be excreted for a while in essentially normal amounts, or perhaps in even larger amounts than normal. Cyclic or acyclic estrogenic bleeding may continue in normal, scanty, or excessive amounts up

*From the Endocrine Division of the Department of Obstetrics and Gynecology, Duke University School of Medicine and Hospital.

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until actual menopause. Menopause itself occurs when estrogenic levels become critically low and cease to be characterized by significant fluctuations.

Hormonology: The changes just described initiate the hormonal alterations characteristic of the climacteric. More profound and general alterations follow.

From the time that sexual maturity was attained, until such time that the climacteric alterations begin, the function of the anterior pituitary is regulated both qualitatively and quantitatively by influences exerted by the ovarian hormones. In a way, the ovaries may be regarded as "governors" of the pituitary. When, due to senility, ovulation and the formation of corpora lutea cease to occur, the gonadotropic influences of the pituitary become fundamentally uniphasic ones characterized by follicle stimulation. As ovarian failure becomes more marked and the follicular apparatus becomes less receptive to these influences, the pituitary, as if to overcome this refractivity, secretes increasing amounts of these follicle stimulating principles with the result that there arises a secondary and compensatory hyperfunction of the pituitary. This over activity of the pituitary, while fundamentally concerned with gonadotropic functions, doubtlessly involves to a varying degree the other tropic influences of the pituitary, particularly the adrenotropic and thyrotropic ones.

Investigation of the hormonal content of body fluids, particularly that of the urine, bears testimony to these aberrations in the endocrine system. Sodium pregnanediol glucuronide (metabolic excretionary product of progesterone) either ceases to appear in the urine or occurs there in very small amounts. Total urinary estrogens decrease gradually but small amounts of these may be found for some years in the urine. As the urinary estrogens decrease gonadotropes appear in the urine and increase *pari passu* with further decreases in estrogens. Positive gonadotropuria may occur for years after the menopause.

In a certain number of patients signs of hyperthyroidism may appear. Since these signs and symptoms are not strikingly different from those commonly considered characteristic of the climacteric under certain conditions, the involvement of the thyroid may be overlooked. Climacteric hyperthyroidism is thought to occur in those women whose thyroids are unduly sensitive to the secondary increase in the thyrotropic activity of the pituitary.

Some workers have emphasized alterations in adrenal function during the climacteric. Some evidence has been submitted that increased activity of the adrenal medulla occurs. Many of the symptoms and signs which climacteric women have are not unlike those produced by large doses of epinephrine. It is difficult, however, to relate a hypermedullary state to the compensatory hyperfunction of the pituitary, for no direct hormonal associations have been established between the adrenal medulla and the pituitary. Alterations in the function of the medulla, when they occur at this time, probably are due to neurogenic factors.

Recently our group[2] has suggested the occurrence of important alterations in the function of the adrenal cortex during the climacteric and has attributed to the adrenal cortex an important rôle in the ultimate stabilization of the endocrine system at this time which results in the advancement of sexual regression and of aging. Many workers in the past three or four years have verified the fact that normal women excrete androgenic principles in amounts comparable to those excreted by normal males. When these reports first appeared, many biologists accepted them with considerable hesitancy for it had been felt that sex was more clearly delineated as regarded endocrine function. In fact, it had been supposed that various sexual inversions might be explainable upon just such endocrine grounds. It is now recognized, however, that normal males and normal females excrete both estrogenic and androgenic hormones.

At first it was assumed that these androgens in the female were formed in the ovary. Our group, however, has shown conclusively that little change occurs in the urinary values for androgens after bilateral oophorectomy. Other workers have made similar observations. Because of this fact and because of the fact that the most significant quantitative changes in the urinary titers of androgens occur in diseases of the adrenal cortex (values are low in Addison's disease and high in adrenogenitalism), it is believed generally now that the primary source of these androgens is the adrenal cortex.

The first reports concerning androgenic titers in senility indicated that these were low. These studies, however, dealt primarily with the male. Our group has submitted recently evidence that urinary androgens increase during the climacteric. We have found the titers may be from three to five times as great in climacteric women as in normal women during the

period of sexual maturity. Our studies are still in progress and continue to bear testimony which supports these observations. On the basis of our present data, it appears that androgens begin to increase during the early stages of the climacteric and apparently reach a peak during the first year or two after menopause. Androgens then slowly decrease in amount, but in women nearing eighty years of age they occur in amounts equal to or perhaps slightly higher than those found in normal women.

These observations have permitted theories which extend the hormonology of the climacteric and of aging women. It is assumed that the ultimate stabilization of the endocrine system is brought about by this secondary hyperactivity of the adrenal cortex. Were not some mechanism present for stabilization, the anterior pituitary's function would continue to increase in an unbridled manner until the pituitary became exhausted and a secondary hypopituitarism intervened. It is well known, however, that hypopituitarism does not characterize the well stabilized post-menopausal woman. The theory is advanced then that increasing androgenic titers take over the rôle of stabilization formerly delegated to the ovaries. Ample experimental evidence exists that androgens do depress the gonadotropic function of the anterior pituitary when they reach adequate concentrations. The increase in these androgens may be due to two distinctly different mechanisms: 1. the secondary hyperfunction of the pituitary which results in increases in adrenotropic influences; and 2. an intrinsic increase in adrenal function due to release from antagonistic influences exerted by ovaries upon adrenals.

It has also been suggested by our group, that the regressional alterations which occur characteristically in the sexual system during the climacteric may be due primarily to the anti-feminizing effects of these androgens, rather than due solely to decreases in estrogenic hormones coincident to ovarian failure. These changes thus are explained as being in part the result of specific pharmacologic activity of androgens. This latter explanation is particularly applicable in instances wherein sexual regression occurs despite the urinary excretion of appreciable amounts of estrogen. The source of this estrogen has been somewhat difficult to explain particularly in women who have had bilateral oophorectomy. Its most likely source is the adrenal cortex and its presence may be due to the hyperfunction of the cortex at this time. Androgens apparently occur in much larger amounts than estrogens at this time.

The somatic changes which occur in senescent women suggest in part a continuation of the effects of these androgens and of other adrenal principles. Among some of these alterations which seem particularly explainable on this basis are: changes in the texture and pigmentation of skin; increase in facial hair; elevation in blood pressure; changes in the voice.

These views, therefore, indicate that the adrenal cortex may play a dominant rôle in the final stages of the climacteric and in the process of aging. One may look upon the period of sexual maturity as being one primarily characterized by dominance of ovarian function, and upon senescence as being an epoch in which adrenal function predominates. The climacteric may be viewed as a period of transition during which the ovaries transfer their dominance to the adrenals. The adrenals may be regarded, therefore, as becoming the gonads of the aging woman.

Symptomatology: There is no strict agreement as to the incidence of disconcerting symptoms in climacteric women. Norris[3] estimated that 90 per cent of healthy women go through the climacteric without experiencing any symptoms which interfere materially with their general health or domestic and social activities. Recent studies from Great Britain have indicated that nearly 90 per cent of women pass through the climacteric without having enough discomfort to disturb their usual daily duties. Most estimates in this country place the incidence of disconcerting symptoms at 15 to 35 per cent of climacteric women. Hawkinson,[4] however, has expressed a contrary view and states that fully 75 per cent of all women suffer distressing symptoms at this time.

It is true, however, that few women have a complete absence of subjective symptoms at this time. Bishop[5] estimated that approximately 15 per cent observed only the menstrual alterations. Mild symptoms related to the vasomotor system and to the psyche occur in most women. These symptoms include: thermic ones, characterized by transient sensations of being either hot or cold; insomnia; and instability of the emotions; a frequently recurring feeling of anxiety and apprehension for which the patient can adduce no cause; a tendency to become confused and disconcerted upon the slightest provocation: languor and fatigue; headaches and vertigo.

It has been said that 20 per cent of women having symptoms at this time have only thermic ones of mild degree.

A relatively few women experience severe symptoms at this time. The lists of these symptoms as given by some writers are formidable and remind one of the humoral pathologist who described "violent cardialgias . . . intense heat and pain about the precordia . . . pain in the joints . . . erysipelatous fever . . . nephritic disorders accompanied with pain in the loin and terminating calculous concretions . . . discharges of bloody urine . . . vomiting of blood or the morbus niger of Hipprocrates", etc.

Among the symptoms which are most commonly encountered as complicating the climacteric are the following: headache; hypertension of a peculiarly labile sort; epilepsy; skeletal ones characterized by arthritis, myalgia, acroparesthesia and neuralgia; and prolonged, too frequent or excessive uterine bleeding.

Etiologic Factors of Symptomatology: We have considered the endocrine alterations which occur in the climacteric. From this consideration it would seem that fundamentally the adjustments are the same in those women whose symptoms are minimal and in those women whose symptoms are more severe. All have the same degree of ovarian failure. All experience the secondary hyperfunction of the pituitary. All eventually become stabilized at a comfortable level. The period of stabilization, however. may vary from a few months to several or more years. Certain endocrine conditions may be suggested as predisposing to prolongation of the symptoms or to producing severity of symptoms. The secondary hyperfunction of the cortex which theoretically may be a stabilizing mechanism may be delayed in its occurrence. Unusually sensitive thyroids may be stimulated to hyperfunction as a result of a compensatory hyperfunction of the pituitary. Unstable adrenal medullae may become hyperfunctional due to the instability of the vegetative nervous system at this time.

There are many other factors which seem particularly implicated in exposing the nervous and endocrine systems to damage at this time. As a rule, a well balanced healthy woman usually has relatively few symptoms. A careful and sympathetic investigation of patients with severe symptoms often reveals definite psychic factors the proper handling of which materially aids in the therapeutic salvage. Among these may be mentioned the following: a phobia founded in general on ignorance of the sexual phenomena and in particular upon an insecurely justified dread of this period of life; sociologic conflicts; domestic infelicity and marital disharmony; financial reverses; defense mechanism against the continuation of sexual relations; an inability to accept the cosmetic alterations of age; improper attention to general health; over-indulgence in stimulants; and a plea for sympathy as a method of retaining the husband's attention. These psychic factors explain the excellent therapeutic results obtained by different physicians employing divergent measures, which include the liberal use of sedatives, psychotherapeutic ventilation and various endocrine preparations.

Diagnosis and Treatment: The diagnosis that a woman is passing through the climacteric is not difficult. The age of the patient, the irregularity or cessation of uterine bleeding, the regressional changes in the genital system and the typical somatic alterations which have come to be associated with the middle aged woman make the diagnosis an easy one. As Ploss and Bartels[6] have observed: "It is possible, on seeing a woman from behind, if artificial appliances do not conceal her from, to hazard an approximate conclusion as to her age."

Diagnoses rest, however, upon very insecure foundations, if it be assumed that all the symptoms which women have between the ages of forty and fifty-five are due to "the change of life". Our diagnostic acumen must be as alert during this span of years as at any other time. Symptoms and signs of intercurrent disease must be suspected, confirmed or ruled out with the same diligence as in the preadolescent girl and in the sexually mature woman.

At the present time when there is such enthusiasm for and such general employment of endocrine principles, it is not unusual to find ovarian hormones almost universally employed in treating climacteric women. Doubtlessly much of this therapy is unnecessary and wasted. Pratt and Thomas[7] have emphasized the rôle which a sympathetic psychotherapeutic approach has in these patients. They have reported therapeutic results which were equally good in patients treated with psycho-therapy and estrogenic principles and in those treated alone by psycho-therapeutic measures.

Estrogenic principles exert specific effects which warrant their use in selected climacteric patients. If

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given in large doses they will overcome and prevent sexual regression, prolong the course of uterine bleeding and prevent the secondary hyperfunction of the pituitary. By producing these effects they may be made to postpone the orderly course of the climacteric and by doing so they do curtail and prevent the associated symptomatology. Treatment of this sort is irrational for there is no more reason for attempting to postpone the beginning of old age than to try to prevent old age itself.

The employment of moderate doses of estrogenic substances to mitigate severe symptoms and to make less rocky the road of the climacteric is rational, if this treatment be not intensive or prolonged enough to materially impede the physiologic process. The oral employment of estriol glucuronide (emmenin), estriol (theelol) or estradiol (progynon-DH) for a few weeks or months frequently constitutes all the treatment which is necessary.

There is another important reason for caution in the use of estrogenic principles at this time of life. There is a growing belief that these substances possess carcinogenic properties when given in large amounts over long periods of time to women unduly sensitive to them. A clearer definition is being gradually evolved in regard to these principles and genital carcinoma. It is commonly said that carcinoma of the cervix or of the uterus never develop in women who have had their ovaries removed. So far the expense of estrogens and the necessity of giving them by injection has prevented women from receiving large doses over long periods of time. In the last year or so certain synthetic estrogenic substances, such as stilboestrol, have been prepared and are being offered for clinical trial in this country. These are not hormones. They do not fit into the endocrine system. They are active by mouth. They will be relatively cheap. It is my personal feeling that their availability for self medication, their activity by mouth and their cheapness may constitute a definite hazard because, then, ideal circumstances will exist for the production of carcinoma. These substances should be tried with caution.

Recently androgenic substances have been used in the treatment of women. They have been employed in practically all the same conditions for which estrogens have been used. This therapeutic excursion proceeded with breath-taking speed, but now caution has become the pass word when most disconcerting virilizing influences such as hypertrophy of the clitoris, hypertrichosis, hoarseness of the voice have occurred and have already led to medico-legal complications. Our theory as to the influence of androgens in bringing about ultimate stabilization of the endocrine system in climacteric women may suggest their therapeutic application. In properly selected patients whose climacteric is lasting unnecessarily long there may be some justification for the use of androgens. The future must determine their value here and weigh it against any possible harmful effects.

A reconsideration of the hyperfunctioning state of the pituitary at this time and of the refractive state of the ovaries should itself sternly refute a wide spread practice of using various anterior pituitary and anterior pituitary-like principles at this time.

Any attempt at therapy should bear in mind the various psychic and nervous factors operative. Measures which quiet and soothe the mind and nervous system are often much cheaper and much more effective than the endocrine principles.

No diligent physician will fail to be on the alert for carcinoma in women during the climacteric. A careful pelvic examination with visualization of the cervix by speculum should be a part of every investigation. Prolonged, too frequent or excessive bleeding should not be treated empirically with endocrine agents or with roentgen therapy without a preliminary study of the endometrium by a competent pathologist.

The physician's rôle in the handling of climacteric women is a clear cut one. Much will be accomplished by the institution of active prophylactic measures as the patient approaches this time of life. Unnecessary damage or sacrifice of ovarian function should be avoided in every female regardless of her age. The general level of health should be carefully guarded as the climacteric approaches. Obesity should be guarded against and treated if it exists, and similarly rest and liberal diet should be assured the woman who is underweight and poorly nourished. A sympathetic conference with the woman which outlines the clinical and biological aspects of the climacteric repays well. The words of Sarah Trent[8] often help in effecting a healthier philosophy and a happy mental orientation: "Let women understand this neat division in their lives—the years up to forty for growing, for learning, for marrying and bearing children; the latter years for self expression

and for herself and for all kinds of social and helpful activities."

Moderate exercise, regular hours of rest and relaxation, avoidance of over indulgence of foods and stimulants, a cheerful environment, a freedom from financial worries are to be desired and are beneficial to the patient if they can be secured.

Summary: Some endocrine, medical and gynecologic aspects of the female climacteric have been considered. These are summarized briefly:

1. A review of the endocrine physiology suggests that the adrenal cortex may play an important part in producing the alterations which characterize the climacteric and somatic aging.

2. A refractivity of the ovaries, due to senility, is the primary cause for the initiation of the climacteric alterations.

3. Many diverse factors, endocrine and non-endocrine ones, operate to aggravate the symptomatology of certain climacteric women.

4. The exercise of an alert diagnostic acumen is essential to evaluate these factors, to exclude the occurrence of intercurrent disease and to outline a therapeutic approach.

5. Organotherapy is only one of various therapeutic measures: only a minority of climacteric women requires it.

6. The prolonged use of large doses of estrogens by injection may unnecessarily prolong the climacteric, and, thereby, aggravate rather than minimize the symptomatology. Often the oral administration of estrogens, such as emmenin, is all the endocrinal therapy that is needed.

7. Androgenic principles and certain synthetic estrogens, such as stilboestrol, should be not employed generally in the treatment of climacteric women until their pharmacology is better known. Gonadotropic principles, regardless of their source, are valueless.

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ULCERS OF THE PYLORIC SPHINCTER WITH CASE REPORTS.*

GUY W. HORSLEY, M.D., F.A.C.S.,
Richmond, Virginia.

Ulcers of the pyloric ring are comparatively rare as evidenced by the fact that from 1920 to 1935 only forty-six such cases were recorded at the Mayo Clinic, according to Butsch, and only ten of these were definitely diagnosed by examination of the specimen removed at operation. The other thirty-six cases had a gastro-enterostomy performed and the operating surgeon made a diagnosis of ulcer of the pyloric ring at operation. As Butsch says, "an exact anatomicopathological diagnosis in this group is, of course, impossible, and uncertain".

A review of the literature shows that little has been written on this subject as very few authors separate this type of ulcer from a gastric or duodenal ulcer. The symptoms are similar to those of other peptic ulcers but accentuated due to their position. These ulcers may be likened to a fissure-in-ano as the pain and discomfort are caused not only by the nature of the lesion but also by its position within the grasp of the sphincter, whose chief function is tonic contraction with only intervals of relaxation.

*From the Surgical Department of St. Elizabeth's Hospital, Richmond, Va.
Presented at the Southside Virginia Medical Association, at Petersburg, Va., June 13, 1939.

From an anatomic standpoint these ulcers are gastric and it is an ulceration of the gastric mucosa. Many of the clinical and laboratory findings are those of a gastric ulcer. Butsch reported that in his series of cases there were 11 per cent achlorhydria with the average free hydrochloric acid being 6.7 units below normal as compared with 5.4 units below normal in other gastric ulcers. In a series of twelve cases reported in 1935 by Dr. J. Shelton Horsley free hydrochloric acid averaged 32.9 with 16 per cent showing achlorhydria. This is 10.3 units below the average.

Nausea with vomiting of large quantities of gastric contents at one time is a frequent occurrence. This seems to be due to the marked retention of gastric contents found in most of these cases, the average amount found in the fasting stomach in these cases being 350 cc. and several cases having 1,000 cc. or more.

The more frequent finding on X-ray examination is almost complete obstruction of the pyloric end of the stomach, there being 70 per cent or more retention at the end of twenty-four hours in one-fourth of Horsley's cases. This was also a prominent feature in Butsch's series. The filling defect seen roentgenologically in most cases is usually absent here because the spasm of the sphincter muscle prevents filling of the ulcer crater.

G. B. Eusteman states: "Apparently the 'syndrome pylorique' is intensified in cases in which lesions are confined to the pyloric ring and it is quite natural that it should be. Of chief clinical interest in this group seems to be the following observations: the comparatively brief duration of symptoms at the time the patient sought relief; the stormy convalescence in the majority of cases, attributed to painful spastic manifestations; the pyloric obstruction of variable degree resulting from spasm, inflammatory reaction, or cicatrization; the dilatation of the stomach even in absence of constant pyloric obstruction; the high volume of gastric content; the preponderance of ulcers in men and the difficulty of clinical and roentgenologic diagnosis so far as actual localization of the lesion to the ring is concerned."

Symptoms in all cases are by no means similar, but they seem to follow the course of other peptic ulcers in periodic discomfort, which may or may not be relieved by food or soda. Roentgenologic diagnosis of unusual spasm or possible obstruction is characteristic, but rarely is found the filling defect supposed to be characteristic of peptic ulcer.

The treatment of this condition is operation. The cases reviewed in the literature and the cases to be reported here have had adequate medical treatment without improvement. The symptoms from this type of ulcer are too severe and the spasm too constant to be relieved by antispasmotics, and anti-acids are of very little benefit as most of these cases already have low acidity.

It is generally accepted that some type of gastric resection is the operation of choice and, of course, if the normal continuity of the gastro-intestinal tract is maintained, better immediate results will be obtained and there is less likelihood of recurrence of gastric symptoms in the future.

After the obstruction and ulcer have been removed by operation the post-operative care is important to insure a comfortable and satisfactory convalescence. In addition to sedatives and fluids it is very essentials to give the stomach adequate rest and to prevent distention. This has usually been done by inserting a Jutte or Levine tube through the nose immediately after operation and aspirate the stomach contents for the first three or four days. In some patients the presence of such a tube is quite a nuisance and often produces a sore and irritated pharynx. To prevent this, at the suggestion of Dr. J. Shelton Horsley, we have been employing a small gastrostomy tube which is inserted into the stomach at the time of operation and brought out through a stab wound in the abdominal wall to the left of the mid line. This gives complete drainage of the stomach and is not as annoying to the patient as the nasal tube. We have been using this gastrostomy tube during the last several months. It is always easily removed without leaving any gastric drainage and the wound promptly heals. These patients should continue on a bland diet for several months, as is the usual procedure following all gastric or duodenal operations, and should have frequent check-up examinations for the first twelve to eighteen months.

I would like to report the following two cases that I have operated upon in the last two years.

Case I. Mrs. G. W., age seventy-two, was admitted to St. Elizabeth's Hospital on January 8, 1937, complaining of a stomach ulcer and vomiting blood. She stated she had had pains in the epigastrium for three months and that there had been a marked loss

of weight during this time. With this had been associated nausea, vomiting, and intermittent diarrhea. Soda, when taken in large doses, gave relief but food did not. She had continued to grow weak and it had been necessary for her to stay in bed three

Fig. 1.—X-ray picture of stomach of Case 1 after taking barium meal; note marked pyloric obstruction and dilated stomach.

weeks previous to admission. Her marital and past history were essentially negative except for having had eight children, and two attacks of kidney colic in the right side during the last five years. Her usual weight was 135 pounds; on admission it was ninety-three.

The examination showed the patient anemic and very dehydrated with signs of marked loss of weight. Heart was normal in size and rhythm; blood pressure 110/80. Abdomen was very relaxed except for spasm and slight tenderness in the upper part of the abdomen. Vaginal and rectal examinations were negative. X-ray examination of the stomach showed definite pyloric obstruction but we were unable to ascertain whether the obstruction was due to an old ulcer or an annular carcinoma of the pylorus. There was a large stone in the region of the gall-bladder—it was uncertain whether it was in the gall-bladder or in the upper part of the kidney. A six-hour X-ray examination showed a 50 per cent retention of the barium meal. Hemoglobin, 32 per cent; r.b.c., 1,980,000; w.b.c., 6,400. Urea, normal; gastric analysis showed a free acid of from four to thirty degrees, total of from twenty-four to forty-two; all four specimens contained blood.

Four days after admission the patient was given a direct transfusion of 500 cc. of blood. She was given daily dextrose in Ringer's solution intravenously, and proctoclysis. She had frequent gastric lavages, leaving in .2 per cent dilute hydrochloric acid after each lavage. Ten days after admission the patient was operated upon under a local anesthetic. The large indurated mass in the pyloric region completely obstructed the gastric outlet. A Horsley modification of a Billroth number one type partial gastrectomy was done. The specimen removed consisted of the pyloric end of the stomach which measured 9½ cm. on greater curvature and 8 cm. on lesser curvative. On opening the specimen, an ulcer was found directly in the grasp of the sphincter. The ulcer measured 2½ x 2 cm. The microscopic examination showed a chronic inflammation with marked fibrosis and areas of degeneration. There was evidence of old hemorrhage but no evidence of any malignancy. The patient was given another transfusion and she made an uneventful convalescence. The stomach was kept empty by a nasal drainage tube. She was first fed on the third post-operative day. She was discharged from the hospital on the twentieth day after operation in ex-

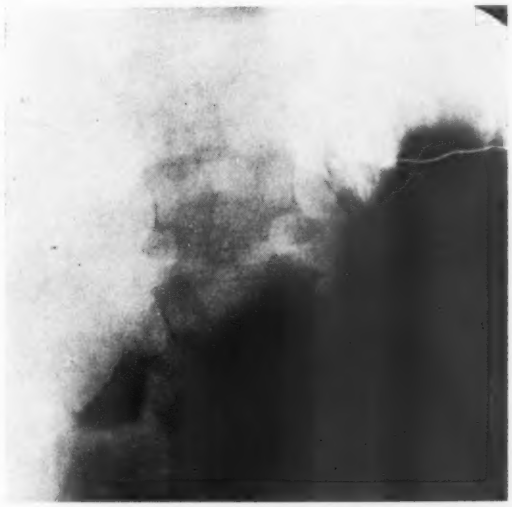

Fig. 2.—X-ray picture of Case 2 showing pyloric obstruction with 50 per cent retention four hours after taking barium meal.

cellent condition. When last heard from, several days ago, she stated she had had no further trouble and had regained her normal strength and weight and was feeling well.

Case II. Mr. J. F., age forty-seven, was admitted

to Sheltering Arms Hospital complaining of sharp epigastric pain which was relieved by soda but not by food. This complaint had been present only a short time and during this period there had been a marked loss of weight. X-ray examination showed a large filling defect in the pyloric region, possibly due to a carcinoma or an old ulcer. The patient's past history was essentially negative except in 1929 he was operated upon for a mixed tumor of the parotid gland and there had been no recurrence. The laboratory findings in this case were essentially negative. The gastric acidity showed an average of 22 units free and 30 units total.

Fig. 3.—Specimen from Case 2 showing ulcer directly in group of pyloric sphincter, another gastric ulcer and also larger gastric erosion.

The physical examination showed the loss of a great deal of weight, definite spasm in the upper part of the abdomen, and tenderness in the region of the duodenum. The examination was otherwise negative.

The patient was operated upon on April 12, 1939, under local anesthesia, using small amounts of nitrous oxide during the last fifteen minutes of the operation. The pylorus was found to be completely occluded by scar tissue. The gall-bladder showed inflammation and contained a small stone. The Horsley modification of Billroth number one type partial gastrectomy was done, removing about one-half of the stomach; the gall-bladder was also removed. The gastric specimen measured 14 cm. on the greater curvature and 6 cm. on the lesser curvature. On opening the specimen the pyloric sphincter was found to be greatly hypertrophied with an ulcer directly over the sphincter. There was another ulcer on the gastric side of the sphincter and a large erosion measuring 4 cm. above the sphincter on the lesser curvature.

The patient made a very satisfactory convalescence. He was discharged on the 24th post-operative day and has had no further complaints. I used the gastrostomy tube described in the first part of this paper with very pleasing results in this case. There was no pharyngitis and when the tube was removed there was no leakage of gastric contents.

These two cases follow the expected course of pyloric sphincter ulcers, having a low gastric acidity, a very stormy and painful pre-operative course, marked gastric retention, and X-ray findings of almost complete pyloric obstruction. Both cases had the significant symptoms of temporary relief by soda, but food gave no relief.

SUMMARY

The exact diagnosis of a peptic ulcer in the pyloric sphincter is rather difficult. The treatment of this condition must be entirely different from the treatment of other types of peptic ulcers. Medical treatment is of very little value and no surgical procedure seems to be satisfactory unless the ulcer and the sphincter are removed, which is best done by a partial gastrectomy. The operation should be followed by careful post-operative attention and the patient should be kept under observation after being discharged.

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RECENT DEVELOPMENTS IN GYNECOLOGICAL ENDOCRINOLOGY.*

JOSEPH A. HEPP, M.D.,
Assistant Professor of Gynecology, School of Medicine, University of Pittsburgh,
Pittsburgh, Pennsylvania.

Historical. Briefly, a few dates in endocrinology are worth mentioning. In 1849 Berthold demonstrated the gonads were endocrine organs. Landau, in 1896, prescribed ovarian preparations in treating amenorrhœa and menopause. Fraenkel, the foster father of the corpus luteum theory of menstruation, experimented with the corpus luteum of rabbits during pregnancy in 1903. In 1917, Stockard and Papanicolaou demonstrated the vaginal spread in rodents. 1927, the Allen-Doisy test. In 1928 Aschheim and Zondek announced their biologic test for pregnancy. In 1929, theelin was isolated in crystalline form by Doisy. Robert Frank, working in the field of gynecologic endocrinology over a period of thirty-five years, demonstrated estrin in the blood and urine of the non-pregnant woman. Frank, by his subsequent work, has shown a definite rise and fall of hormones in the blood and urine during the normal menstrual cycle, and he has contributed much in amenorrhœa and the menopause.

PITUITARY-OVARIAN-UTERINE RELATIONSHIP IN THE NORMAL MENSTRUAL CYCLE AND IN PREGNANCY

The endocrine glands are interrelated to each other and maintain a balanced system; when this endocrine chain is broken or when this balance is interrupted, certain physiological, anatomical and chemical changes manifest themselves.

The hormones which originate in the anterior lobe of the pituitary are:

1. Growth hormone—secreted by the acidophile cells.

2. Gonadotropic hormones—secreted by the basophile cells and chromophobes.

   A. Follicle stimulating hormone.

   B. Luteinizing hormone.

3. Lactogenic hormone (prolactin) — influences lactation following estrogenic breast stimulation.

4. Mammogenic hormone—influences growth of the duct and acinar system of the breasts during pregnancy.

5. Thyrotropic hormone—influences thyroid activity.

6. Adrenalotropic hormone — influences adrenal activity (cortical portion).

7. Metabolic hormones—influences pancreatic activity.

   A. Blood sugar raising hormone.

   B. Fat metabolism hormone.

In the normal menstrual cycle, the follicle stimulating hormone of the anterior lobe stimulates follicle ripening and the follicle of the ovary secretes "estrin" which causes growth and vascularization of the uterine musculature and swelling of the endometrium. This comprises the follicular phase of the cycle or "priming of the endometrium".

The luteinizing hormone of the anterior lobe has its effect on the ruptured Graafian follicle and produces the corpus luteum. The corpus luteum, in turn, secretes the hormone "progesterone", as well as "estrin". Progesterone changes the follicular endometrium to the luteal phase which is necessary for nidation and early nutrition of the fertilized ovum. In the normal menstrual cycle with regression of the corpus luteum, there is a cessation of estrin and progesterone production and consequently menstruation occurs. As you know, in pregnancy the hypophysis is very active and the hormones in the urine are similar to, but not identical with, the anterior lobe gonadotropic hormones. These hormones, in pregnancy urine, are called anterior pituitary-like substances and are produced by trophoblasts at the site of the placental development. The Aschheim-Zondek pregnancy test is positive if active trophoblastic tissue is in contact with the circulation.

The Aschheim-Zondek Test. This biologic test for pregnancy is really the only worthwhile product of the intensive work in female reproductive physiology over a period of the last twenty-five years. For practical purposes, biologic diagnosis of pregnancy is especially desired during the first few weeks. In our series, extending over eight years, we have completed 1,000 pregnancy tests, 845 mouse tests and

*Read before the joint meeting of the West Virginia Obstetrical and Gynecological Society, and the Pittsburgh Obstetrical and Gynecological Society at Magee Hospital Pittsburgh, Pa., April 3, 1939.

155 rabbit tests (Friedman). The test checked accurately with clinical observation in 95.4 per cent of cases. How early in pregnancy did the reaction become positive? The test was positive when the urine was examined eight days after the menstrual period was due and at this time the pregnancy was twenty-two days old. Subsequent clinical observation confirmed the test. In another case, the urine was positive before a laparotomy was done for ectopic pregnancy. Here, the clinical history revealed no missed period but the patient had spotting for six days after the last menstrual period and the spotting was accompanied by cramps in the lower abdomen. Of the numerous modifications of the Aschheim-Zondek test, not one has any special advantage or has been generally employed except the method of Friedman, in which mature female rabbits are used.

Two very common gynecologic disorders for which a patient seeks advice are functional uterine bleeding and the menopause.

Functional Uterine Bleeding. The endocrine mechanism concerned here usually causes an alteration from the normal relationship between the hypophysis, ovaries, thyroid and the endometrium. Other glands may be involved. Endometrial biopsy studies have shown that excessive menstruation can occur from almost any type of endometrium. The endometrium, most characteristically, shows hyperplasia, especially cystic in type, but often it is atrophic or in a resting stage. Since this type of hemorrhage is sometimes associated with various degrees of hypothyroidism, a B.M.R. determination should always be run, and we must always remember the value of desiccated thyroid, even in the absence of definite evidence of deficient thyroid function, both clinically and by B.M.R. determination. Thyroid gland substance, administered in conjunction with other hormone products, particularly the chorionic hormones as A.P.L. (Ayerst) is of definite value. Novak has repeatedly said that thyroid is the sheet anchor of endocrine therapy.

What is the treatment of functional hemorrhage from puberty through the child-bearing age? Conservatism is the keynote at this time of life. Aside from endocrine therapy, the patient must be treated for hemorrhage. Blood transfusion and iron therapy are of definite value here. Currettage may stop the bleeding. As I mentioned above, thyroid therapy is of definite value in adolescent bleeding. While speaking of treatment, we cannot forget that often the bleeding will stop spontaneously, without any treatment whatsoever. Chorionic hormones, which enjoy wide usage in functional bleeding at the present time, are A.P.L., follutein and Antuitrin-S. Before and during the reproductive ages, the maintenance of menstrual and reproductive functions demands a trial of conservative measures.

Should glandular products be given in premenopausal or menopausal bleeding? No, because cancer should always be ruled out by a diagnostic curettage. Here radium or surgery solves the problem and the results are more satisfactory than in the child-bearing age.

The Menopause. Many women pass through the menopause with few symptoms, and they need no treatment. In another group of women the symptoms are rather mild, so that no treatment is necessary except a reassuring and confidential talk by the physician as to the nature of the symptoms, the importance of avoiding stress and anxiety and perhaps the administration of simple sedatives as luminal, bromides or phenobarbital. You are all familiar with this type of patient. What are the characteristic symptoms of the menopause? There is only one group of symptoms to which all agree, i.e., vasomotor phenomena as periodic flushes and sweats and also the flashes of heat which may involve the entire body. Very often these hot flashes are confined to the neck and face and head. It is surprising to know that the brilliant advances made in reproductive physiology have added little to our knowledge concerning the mechanism of these menopausal vasomotor phenomena. We all know that after bilateral oöphorectomy or after destruction of the ovaries by cystic changes, these vasomotor phenomena manifest themselves. In the light of recent advances in endocrinology, what is the mechanism? There is a decrease and finally stoppage of ovarian function and there is an increase in anterior lobe activity as shown by urine gonadotropic hormone studies. What basis have we for the use of estrogenic substance here? Follicular hormone is of value for two reasons: 1. We know that the menopause is produced by the withdrawal of ovarian secretions. 2. Since complete cessation of ovarian function always induces hyperactivity of the anterior lobe of the hypophysis, it seems plausible to ascribe these vasomotor disturbances to an excess of anterior pituitary hormones.

Therefore, it seems logical to attempt an inhibition of anterior lobe over-activity by means of follicular hormone.

The etiology of functional bleeding at the age of thirty-two is different from the etiology of the bleeding at age forty-eight. Although there is absence of lutein tissue at both these ages, we all know the absence during the child-bearing period is only temporary. However, in climateric bleeding, because the ovary has lived its physiologic life span, it is unable to form lutein tissue. In climacteric bleeding, there is a decline in ovarian function, due to intrinsic structural changes in the ovary as shown by the increased function of the gonadotropic hormone of the anterior lobe. This is proved by the presence of large amounts of follicle stimulating hormone in the urine, but in the urine hormone tests in bleeding at age thirty-two there is absence of anterior lobe hormone. Although diagnostic curettage in both instances may show cystic endometritis, the etiology and the results from hormone studies are somewhat different.

In recent work by Frank and his co-workers, hormone studies showed that cessation of ovarian function is followed by persistent over-secretion of follicle stimulating and also luteinizing gonadotropic factors of the pituitary. He has also demonstrated that injection of the estrogenic factor, in proper dosage, temporarily overcomes the excessive anterior lobe action with rapid disappearance of both factors from the blood and urine. Although most of the evidence today is in favor of decreasing ovarian function as the prime factor in causing the hot flashes, other investigators believe that the vasomotor symptoms are due rather to gonadotropic excess than to the estrone deficiency.

From this you can see, although the etiology is still an unsolved problem, the administration of estrogenic substances in the menopausal patient is certainly in keeping with present-day physiologic knowledge.

In evaluating the results from follicular hormone therapy, we should be guided by the decrease in severity of the vasomotor phenomena. Another guide in treatment has been the vaginal spread method, as demonstrated by Papanicolaou and Shorr. In regard to dosage and treatment, common sense should be the rule; for example, if 5,000 international units do not give relief, the dosage may be increased to 20,000 or 50,000 units, etc. This rule of increasing dosage should apply to oral medication. The oral route is very popular today and is usually sufficient in the milder symptom patient. In patients with severe vasomotor symptoms, the hypodermic route secures better results and is much more effective, especially in the beginning, because, later on, these patients can be treated by the oral route. Novak has said that organotherapy must be combined with intelligent management of the particular woman's entire menopausal syndrome. For example, in some women the fear of cancer may be in the background; in others, a fear of pregnancy or insanity. All these factors should be confidentially discussed and their correction must constitute a part of the management of such cases.

Results. Over a period of ten months we have treated thirty-three menopausal patients in the gynecological endocrine clinic of the Magee Hospital. These patients fall into five groups: hysterectomy; hysterectomy with bilateral oöphorectomy; hysterectomy with unilateral oöphorectomy; radium; and normal non-surgical menopause. Because hot flushes are such a constant symptom of the menopause, no patients were included, in this series, who did not have this symptom. The highest number of hot flushes and sweats per week in this series was 180 in a patient who had a bilateral oöphorectomy for extensive pelvic endometriosis. This patient was given 30,000 international units of estromone* in oil every other day for several weeks until she showed signs of improvement and now she is being treated with 10,000 units of estromone once a week. Another patient, who had radium castration, was given 20,000 units of estromone a week for three weeks, after which the dosage was reduced to 10,000 units of estromone a week and at the present time this patient receives 5,000 units every three weeks. The number of hot flashes at the beginning of the treatment was 110 a week and now it is twenty-one per week. This patient has been under treatment for eight and one-half months. A third patient was in the normal non-surgical menopause group with hypertension, the blood pressure before treatment being 185/95, during treatment 180/112, 202/100. Under treatment her hot flashes decreased in number and she felt better, but as you see, her blood pressure was not decreased. In other words, the hypertension was unimproved

*Dr. Samuel Gordon, of Endo Products, Inc., has generously supplied us with estromone.

by the treatment which was effective on the other symptoms.

Another patient, when first seen, showed 10 R.U. urinary gonadotropic factor and after she was given 20,000 units of estromone, the gonadotropic factor was reduced to one. With this decrease in anterior lobe activity there was a decrease in the number of hot flashes.

Three patients, in this series, who had radium castration, received considerable relief from the hot flashes with progynon B, theelin in oil and emmenin, and emmenin alone. One of these patients said she was free of symptoms as long as she took emmenin but as soon as she stopped taking this medication her symptoms returned and became increased. Two other patients had their symptoms controlled entirely with oral medication, emmenin and progynon D H tablets. Sometimes it was necessary to use a combination of oral medication and intramuscular injections.

Although these patients are still under treatment, they are all improved, and the number of hot flashes has decreased. These symptoms increase as soon as treatment is withheld.

SUMMARY AND CONCLUSIONS

The Aschheim-Zondek test continues to be a reliable test when checked by subsequent clinical observation.

Pregnancy urine preparations as A.P.L., follutein and Antuitrin-S are of value in functional uterine bleeding during the reproductive stage of life.

Preparations used in treating a series of thirty-three menopausal patients were: oral preparations in this series consisted of emmenin, estradiol (progynon D H), and estrone (amniotin); the hypodermic preparations were estromone, estradiol benzoate (progynon B) and estrone (theelin).

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121 University Place.

PLACENTA ACCRETA: BRIEF SURVEY OF LITERATURE, WITH REPORT OF CASE.*

JULIEN H. MEYER, M.D.,
and
JOHN W. ASHWORTH, JR., M.D.,
Baltimore, Maryland.

DEFINITION:

Placenta accreta is an abnormal condition of the after-birth, in which it is attached, either wholly or partially, to the underlying wall of the uterus; the villi attach themselves directly to, or even penetrate into, the uterine muscle. The decidua basalis, especially its spongy layer, is usually absent, to a greater or lesser degree.

INCIDENCE:

The figures vary widely. B. C. Hirst reported one case in 40,000 deliveries. Phaneuf placed the incidence at one in 14,622 deliveries; his average was obtained from all available statistics at that time (1933). Lawson and Oginz concluded from statistics and their own cases that placenta accreta occurred in one case in 13,500 deliveries. Incidence of Irving and Hertig was given as one case in 1,956. In our review of the literature, we have been able to find a total of 118 cases reported. At St. Joseph's Hospital in the last ten years there was one case in 9,176 deliveries.

The cases of placenta accreta reported have occurred almost entirely in multiparous women.

ETIOLOGY:

Most probable causes, in order mentioned:

1. Previous manual extraction of placenta.

2. Curettage—too thorough curettage, when only a little endometrium is left for regeneration.

*From the Gynecological Service of St. Joseph's Hospital, Baltimore, Md.

3. Endometritis.
4. Submucous fibroids.
5. Atmocausis (historical).
6. Previous caesarean section. This is a mechanical factor given as possible cause by King.

Theories:

a. Inflammation.
b. Bleeding in early months of pregnancy.
c. Deportation of villi via blood stream.
d. Endocrines.—This would naturally be the latest theory. Faulty implantation of the placenta results from imperfect development of the mucosa and this in turn is due to a hyper- or hypo-secretion of one of the sex hormones, possibly a lack of corpus luteum.

PATHOLOGY:

In the normal third stage of labor, the placenta separates in the spongy layer of the serotina (Langhans'). As no spongy layer exists in placenta accreta, separation cannot take place; the myometrium and villi are fused and there is no line of cleavage.

With either the incomplete or complete absence of the decidua basalis, the villi follow the trophoblasts and penetrate the muscle, which usually undergoes degeneration. There is excessive thinning of the uterine wall.

Fig. 1.—Gross specimen of uterus with attached placenta.

Irving and Hertig state that deep penetration of the villi was not a feature of their cases, nor was excessive thinning of the uterine wall that so often accompanies it. They found evidence of chronic inflammation of the decidua in six of their cases, and acute inflammation in two of them.

Summary of pathological findings in the literature:

1. Total or partial absence of whole decidua basalis.
2. Absence of either spongy or compact layer.
3. Penetration of epithelial cells, probably of a trophoblastic nature.
4. Deep penetration of chorionic villi into the uterine wall. Nathanson states that he did not find any deeper penetration into the uterine wall than one would encounter on study of the normal placental site.
5. Thinning of the uterine wall.
6. Changes in the layer of Nitabuch.
7. Myometrial tissue drawn up into the decidual septa.
8. Degeneration of the myometrium.
9. Acute and chronic inflammation.
10. Increased connective tissue formation.
11. Condition of the decidua vera: some found it normal; others, absent, or poorly developed. The spongy layer was deficient or absent.

Some use the term placenta increta in those cases where the erosive process of the trophoblast has penetrated deeply into the muscularis and even to the serosa.

DIAGNOSIS:

1. One to two hours following delivery there is retention of the placenta.
2. The following classical signs of placental separation fail to become evident:
   a. Bloody show. (If separation is partial, bloody show is present and profuse hemorrhage may occur).
   b. Rise of the fundus.
   c. Descent of the umbilical cord.
3. Manual exploration of the uterine cavity (under strict asepsis) reveals no line of cleavage between placenta and uterus.

TREATMENT:

In our opinion, the accepted treatment is as follows: A manual exploration of the uterine cavity under the most strict aseptic technique is done; however, we feel that this procedure should be carried out in the operating room, when the operating team is prepared for immediate laparotomy. If a line of cleavage can be found and the entire placenta re-

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moved, no further operative procedure will be necessary. If not, the diagnosis of placenta accreta is confirmed and a supravaginal hysterectomy with blood transfusions during and following the operation is indicated.

Fig. 2.—Cross section of uterus and attached placenta, showing that for approximately one-half its breadth there is no line of cleavage.

In the literature, treatment consisting of supravaginal hysterectomy with no attempt at extraction had no cases of mortality. Those cases treated by manual extraction or curettage presented a mortality of 58.8 per cent; those by partial manual extraction and vaginal hysterectomy, 36.4 per cent; partial manual extraction and supravaginal hysterectomy 18.9 per cent.

We conclude, therefore, that if the diagnosis is reasonably certain, the most satisfactory mode of treatment is that of supravaginal hysterectomy without an attempt at extraction of the placenta.

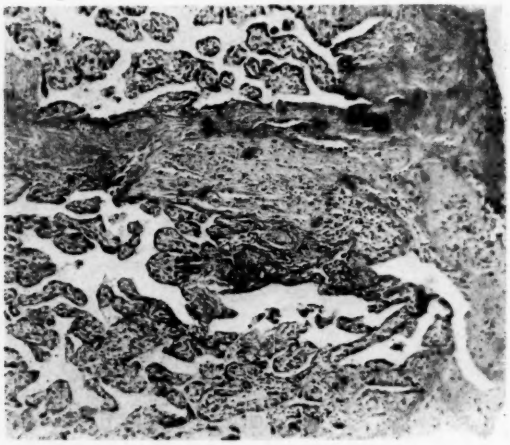

Fig. 3.—Photomicrograph showing thinning out of decidua and the presence of smooth muscle fibres adjacent to the placenta. The placental septae show the myometrium to be present in the placenta.

ABSTRACT OF OUR CASE

The patient, Mrs. B. W., was admitted to St. Joseph's Hospital on the Gynecological service of Dr. Thomas K. Galvin at 11:50 P. M. on December 2, 1938. A note at that time revealed that she had been delivered of a living female child, weight five pounds, one ounce, at 9:15 P. M. Following the delivery the placenta could not be expressed. After about two hours had passed in which there were unsuccessful attempts made at expressing the placenta, including manual exploration of the uterine cavity under non-sterile technique, the patient was sent into the hospital. There had been no administration of oxytocics or anesthetics prior to her admission. There was marked vaginal bleeding and the umbilical cord projected from the vagina on admission. Attempts to express the placenta by modified Crede method were futile. A tentative diagnosis of placenta accreta was made and the patient was prepared for the operating room, after 500 cc. of 10 per cent glucose were given intravenously.

SYNOPSIS OF HISTORY:

Chief Complaint was retained after-birth following a normal delivery.

Family History was irrelevant and past history non contributory except that the patient had had no previous operations or serious illnesses.

Catamenia: Menarche at thirteen years of age; periods regular every thirty days and last five days. Has moderate dysmenorrhea, but no menorrhagia or metrorrhagia. Last menstrual period was March 17-22, 1938.

Marital: Married twice. First husband dead; one child by him. Second husband living and well. This is her second pregnancy; no abortions. First child was a forceps delivery following prolonged labor and ante-partum bleeding, but puerperium was uneventful.

Present Illness: Patient went to a physician when five months pregnant; no examination was made by him at that time. Prior to this, however, she tried to interrupt her pregnancy at two months by taking "Dr. Douglas' Powder", "Dr. Hooper's Green Seal Pills", turpentine, and other proprietary medicines, plus three "hypodermics" given by a physician. Her pregnancy was uneventful.

Labor was normal with no sedation, although the duration was eighteen hours. Delivery was spontaneous. After delivery, placenta could not be ex-

pressed and manual removal was attempted by the accoucheur. As this failed and patient was bleeding, hospitalization was resorted to.

PHYSICAL EXAMINATION:

T. 100. 6; P. 104; R. 22; B. P. 50/30.

Patient was a twenty-year-old, fairly well-developed, well-nourished white female, lying in bed in a shocked condition. Pulse was fast and of poor volume. Skin was pale, cool, and moist. Mucous membranes were of poor color. Head, neck, lungs, and heart were normal. Abdomen—uterus was at level of umbilicus; otherwise, normal. Laboratory findings: Hemoglobin 42 per cent; R.B.C. 2,400,-000. Urinalysis negative.

COURSE IN HOSPITAL:

Patient was taken to operating room, and, under strict aseptic technique, attempt was made to remove the placenta manually. No line of cleavage could be found. Patient was further prepared and under general anesthesia of nirous oxide, oxygen, and ether, she was operated upon. A supravaginal hysterectomy was done, and the abdomen closed with one cigarette drain left inside the peritoneum. Intravenous fluids were given on the operating table, and the immediate post-operative condition of the patient on leaving the operating room was good. Several hours later, patient was given 500 cc. citrated blood transfusion. Her post-operative course was entirely uneventful, and afebrile after the fourth day! Another transfusion was given and incision healed rapidly per primum. Patient was discharged on the fourteenth post-operative day in excellent condition.

PATHOLOGICAL REPORT

Pathological report by Dr. R. B. Wright:

Gross pathology consists of the uterus, attached to the endometrial surface of which there is a placenta.

Microscopic pathology: The sections show a narrow strip of decidum, separating the chorionic villi from the uterine muscle. In some places the chorionic villi are adjacent to the myometrium. In other places there are projections of this hyalinized deciduum extending into the placenta proper. There is no evidence of malignancy.

Pathological report with Mallory stain by Dr. L. M. Hellman:

There are several sections of placenta attached to the uterine wall. The villi are of normal size and show no pathological change. The chorionic plate shows the usual degenerative changes and there is no evidence of inflammatory reaction. There is a pronounced defect in the decidual plate with a great diminution to absence of decidual cells. In many places, a layer of fibrinoid with scattered trophoblast cells is all that covers the myometrium. In areas, the placental surface of this fibrinoid shows infiltration of polymorphonuclear leucocytes. The placenta septae show the myometrium to be present in the placenta. It is quite obvious from the sections that no good line of cleavage could ever have been found. The presence of smooth muscle fibres adjacent to the placenta and in the placental septa is especially well demonstrated. In several areas there are numerous placental site giant cells extending approximately one-third the way into the myometrium. Of special interest is the decidua adjacent to the placenta. The decidua is somewhat thinned out, but no definite areas of absence or scarring could be demonstrated.

Diagnosis: Adherent placenta (placenta accreta).

SUMMARY

1. A case of placenta accreta is presented to be added to the 118 cases already reported in the literature up to the present time.

2. No attempt has been made to clarify the etiology of the condition.

3. From a review of the mortality resulting from the various forms of treatment, it seems clear that supravaginal hysterectomy is the most satisfactory method. No attempt should be made to extract the placenta manually before hysterectomy, if the diagnosis is reasonably certain without carrying out this procedure.

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1400 Caroline Street.

TREATMENT OF GONORRHEA IN THE MALE WITH SULFANILAMIDE AND URETHRAL INJECTIONS OF ACRIFLAVINE.*

WALTER M. BRUNET, M.D.,
CHARLES H. REINHARDT, M.D.,
NORMAN D. SHAW, M.D.,
Chicago, Illinois.

During the last half century every conceivable form of therapy has been recommended for the cure of gonorrhea in the male. Within the past decade biologic control has ridden several waves of popularity but it went out with the tide. Within the past three years sulfanilamide has been acclaimed the "therapia sterilisans magna" in urological practice and physicians have literally deluged the editors of medical journals with clinical reports of their results with the use of the drug.

Lack of acceptable standardized methods of treatment of gonococcal urethritis and unsatisfactory results obtained with most methods, in a large percentage of cases, have stimulated the search for a remedy which would speedily render the patient noninfectious and by continuation of the treatment effect an early cure. This is what happens with syphilis by modern treatment methods. We have had no remedies which approach such control in gonorrhea.

Syphilologists are in complete agreement that a minimum of twelve months of active treatment is necessary for the control and cure of early seronegative or sero-positive lues, and for late and central nervous system involvements years may be required. Urologists rarely see a patient with gonorrhea who requires twelve months of treatment and the great majority are completely recovered in three or four months. However, every gonococcal infection is potentially severe and many first infections are vicious, especially in blonds. There are many physicians who cling to the ancient thought that a Neisserian infection is a passing incapacity rather than a potentially severe disease. Gonorrhea outranks syphilis in its prevalence more than four to one and the actual mechanics of its treatment are as involved and difficult as syphilis. The number of physicians who understand the fundamentals of syphilis and its therapy is not large but there are in proportion just as many poorly qualified physicians who will accept and treat patients with gonorrhea. Most general practitioners, certainly those in the smaller cities, will without hesitation accept for treatment a patient with gonorrhea even when they hesitate to treat syphilis. Both infections can be satisfactorily treated if the physician has not reached the "fixed period" in life and will apply himself to the study of these diseases. The treatment of syphilis is more than being skillful with a needle and making an intravenous injection without infiltrating the arm, so the treatment of gonorrhea is something beyond an urethral syringe and a colored antiseptic solution. The prevalence of both of these infections is so great that there are not enough specialists to adequately treat the numbers requiring care. The time has long since arrived for general practitioners to know how to diagnose and adequately treat these infections. In the complicated cases the expert must be consulted. In gonorrhea as in syphilis the patient must be treated, not just his infection, and this is especially true when a drug as toxic, and as variable in its action on individuals as is sulfanilamide is used. The idiosyncratic, or allergic, reactions produced by sulfanilamide fortunately disappear upon its withdrawal in the vast majority of patients, but in this instance as in the use of arsenic for syphilis the power to control the disease carries with it potential dangers to the blood making organs.

A year ago we published a preliminary report† and warning regarding the use of large doses of sulfanilamide in the treatment of gonorrhea and at that

*From the Urological Division of the Public Health Institute, Chicago, Illinois.

†Brunet, W. M., Shaw, N. D., and Reinhardt, C. H.: The use of Sulfanilamide in Gonorrhea in the Male. *New Eng. Jour. of Med.,* Vol. 218, No. 7, February 17, 1938.

time stated: "We believe that sulfanilamide is, and should be, regarded only as an experimental and speculative remedy until a larger number of adequately controlled and correlated clinical studies have been reported." We think our statements were pertinent then and have since been confirmed. At this time no one knows how sulfanilamide aids in the control of gonorrhea in those patients who are benefited, or why it fails in others. By some it is said to be bacteriostatic, others think that it is bacteriocidal and still others state that it neutralizes toxins. All may be right. There is no doubt that it is a valuable addition to our materia medica, but how great a boon it will eventually prove to be no one can predict. It can be said with emphasis that *the drug is not a specific for gonorrhea in any sense of the word.* Our experience with sulfanilamide extends over a period of nearly two years and we find it difficult to be too sanguine over the good results, or to condemn it too violently when it failed in its action. Some months ago we treated 200 cases of gonorrhea in the male, half of them received twenty grains of sulfanilamide daily and the other half forty grains of the drug daily. We also used local injections of a mild acriflavine solution. The purpose of these observations was to determine the effect of small and moderate sized doses of sulfanilamide on the course of acute anterior and complicated gonococcal infections in unselected ambulatory patients. In the first group, those receiving twenty grains of sulfanilamide daily, 90 per cent reported for treatment within the first week of their infection, and of this number fifty-five were first infections, thirty-one second infections, ten third infections, three fourth infections and one the seventh infection. Of the forty-five patients with a history of previous infections twenty had a complication: they were four acute prostatitis; four prostatitis and epididymitis; four epididymitis; one bilateral epididymitis; two peri-urethral abscess; one arthritis; and four stricture. There were thirty-one cases admitted with a posterior extension and twenty-eight became complicated while under treatment. Thus 59 per cent of this group had a complicated infection. We consider the disease to be complicated when the second urine becomes slightly hazy even if there are no subjective symptoms. The diagnoses were eighteen prostatitis; four epididymitis unilateral; two epididymitis bilateral; three peri-urethral abscess; and one arthritis.

The patients with an anterior infection were placed on small urethral injections of 1-4000 aqueous solution of acriflavine administered daily in the clinic only for the first two weeks. The injections were given with a 10 cc. bulb type syringe and were carried out as follows: The patient urinates in two glasses and the syringe is filled with the solution and about one-third of its contents is slowly injected into the urethra (if the organ is of normal size; if small, a less amount), the medicament retained momentarily and then allowed to escape. This procedure is repeated a second time and the remaining one-third is retained for three minutes. We use an inexpensive three-minute sand glass for the timing. If there are any complaints such as irritation or burning the patient is instructed to expel the solution at once. If the patient develops a posterior extension local treatment is stopped and intramuscular injections of a foreign proteid are given at forty-eight hour intervals for six or eight visits until the second urine clears and remains so for one week when local treatment is resumed. After two weeks of daily treatment, the discharge lessening, we prescribe for use at home an aqueous solution of 5 per cent mild silver proteinate in 4 per cent gelatine. This preparation will gel at a temperature of 50 degrees F. and must be warmed before it is used and the patients are instructed to place the bottle in hot water to liquefy it. A bulb type urethral syringe, previously mentioned, is also prescribed and the patients are instructed to use the treatment once daily, preferably in the evening hours, and not to urinate for one hour after the treatment but to void before retiring. The physician attending the patient stresses the dangers of forceful injections and urges care and gentleness in the use of the syringe, demonstrating repeatedly how the treatments are to be made. After home treatment is prescribed the patient visits the clinic three times a week for a fortnight and if his progress is uninterrupted through the fourth week he reports twice a week. At the end of the sixth week if both urines are clear and the discharge minimal the prostate is massaged and the secretion examined. If the slide shows less than 10 per cent pus cells per high power field and no gonococci, treatment is continued and at the end of a week a straight sound—size twenty-four, if the meatus will admit it—is passed to the bulb. If there is no reaction following this instrumentation the procedure is repeated within three days. If there is no discharge within five days following, the second

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straight sound—a twenty-six Van Buren if the orifice is adequate—is passed into the bladder. This procedure is repeated again within five days. After the use of the two straight sounds acriflavine is instilled into the anterior urethra and both anteriorly and posteriorly when Van Buren sounds are used. All home treatment is discontinued after the second Van Buren sound. Following each of these four tests of cure a glass slide is given the patient to secure any discharge the morning following instrumentation and return it for examination at the next visit. (We have not had a so-called urethral chill for years and only rarely do we have a patient who faints or complains of nausea. When an aseptic technique is strictly followed the reactions will be rare.) If all goes well the next procedure is the instillation into the urethra, anterior and posterior, of a solution of one-half per cent silver nitrate, one week following the last sound. When this provocative is given, the patient is instructed to disregard all discharge which may occur for the first forty-eight hours, but any material which he may secure afterward by gently stripping the urethra is to be placed on a slide and brought in for examination. A routine blood Wassermann is taken on admission and blood is drawn for a second Wassermann at this time. Should these procedures all prove negative a specimen of semen is requested and brought in within a week. We advise that this be obtained manually, be kept warm and examined within four hours. If the microscopic examination of the semen shows it to be normal the patient returns in three weeks for his final examination before he is discharged. Upon dismissal from treatment each patient is advised to return in three months for a re-examination.

Many patients ask at the time of their dismissal from treatment when it will be safe for them to have intercourse, or to marry. We urge that no sexual relations be had for several months and that for six months no intercourse be had without a condom. We advise those who contemplate marriage to delay it for at least six months. There were ninety-two patients in the group receiving twenty grains of sulfanilamide daily who completed all of their tests of cure, and eight became delinquent but were apparently non-infectious when they dismissed themselves. The length of time these patients were under treatment and observation is shown in the accompanying table.

Our tests of cure as outlined above require about six weeks for their completion and this includes a period of three weeks during which time the patient receives no medical attention before the final visit and discharge. With this plan of management 56 per cent of this group of patients were discharged cured within twelve weeks, and an additional 31 per cent at the end of the twentieth week. These results even with our small doses of sulfanilamide compare favorably with those results secured by Bogaev and his associates at the Jefferson Hospital in Philadelphia.* They reported a series of seventy-six patients, of which fifty-six completed their treatment, and of these forty-one, or 73 per cent, were classified as failures and fifteen cases, or 27 per cent, were cured. They used eighty grains of sulfanilamide daily for two days, sixty grains for five days, forty grains for seven days and twenty grains thereafter, and no local treatment was given. These authors do not state the number of cases which were susceptible to the medicament but one patient developed agranulocytic angina and is still under treatment. There were 11 per cent of our patients found to be sensitive to the small dose of twenty grains daily which this group received and 6 per cent of the patients could not tolerate it. Two patients stated that they had the same sensations after taking the drug that were experienced after the use of alcohol and both complained of inability to judge distances accurately while driving their automobiles. One demolished the front of his garage and the other damaged a fire hydrant. The records of ninety-two patients showed that they completed all of their tests of cure, and eight became delinquent but were presumably non-infectious when they dismissed themselves.

The second group of 100 cases received forty grains of sulfanilamide daily. Of this number eighty-three patients reported for treatment within the first week and seventeen patients after this period.

*Bogaev, Litt and Davis: Sulfanilamide in the Treatment of Gonorrhea in the Male. *Jour. of Urol.*, Vol. 41, No. 1, 1939.

TABLE I
PERIOD OF OBSERVATION
(20 gr. sulfanilamide daily)

Weeks	6	7	8	9	10	11	12	13	14	15	16	17	18	20	21	22	24	25	27	32	34
No. of cases	2	1	3	7	22	9	12	7	6	4	5	3	2	4	4	1	3	1	1	2	1

There were two patients that had received treatment elsewhere for six months prior to our examination. There were forty-eight patients who admitted a previous infection, and of these twenty-four gave a history of a complication, viz.: prostatitis ten, epididymitis and prostatitis six, epididymitis and stricture five, bilateral epididymitis two, peri-urethral abscess one. On admission eighteen of the number were found to have a posterior infection and fifteen developed a complication under treatment; thus 33 per cent were complicated. The posterior extensions which occurred while under our care were recorded as follows: prostatitis twelve, epididymitis one, arthritis one, peri-urethral abscess one. In the complicated cases, especially epididymitis, if pain is a disturbing symptom we find intravenous injections of sodium iodide, one or two grams, given every forty-eight hours for several visits a valuable remedy. We prefer heat in any form to cold for local applications in all cases which require it, as facilities are usually at hand in every household and it is better tolerated by the patients and the end results are most satisfactory.

The period of treatment in this second group of 100 cases receiving forty grains of sulfanilamide daily was considerably shortened by the increase in the amount of the drug given. In this series 82 per cent of the patients received all tests of cure and were discharged cured in twelve weeks and only 18 per cent were under treatment beyond this time. The details are recorded in Table II.

TABLE II
PERIOD OF OBSERVATION
(40 gr. sulfanilamide daily)

Weeks	8	9	10	11	12	13	14	15	16	17	18	19	21
No. of cases	13	20	18	12	19	5	3	3	1	1	3	1	1

Sulfanilamide was administered throughout the course of the infection up to the beginning of the tests of cure. We discovered 24 per cent of this group of patients exhibited some susceptibility to the medicament and 10 per cent were intolerant to it and it was omitted. We observed two patients with temperatures above 103°F., six with marked dermatitis, and a number showed minor toxic manifestations. Usually all of the untoward symptoms cleared up promptly when the drug was withheld. We did not make routine blood counts or blood concentrations. The several ill patients on whom complete blood counts were made showed no evidence of blood dyscrasias.

From a diligent study of the literature we do not think that oral administration of sulfanilamide alone should be relied upon to control or cure gonorrhea unless the patients are hospitalized and kept under rigid supervision. Obviously such a procedure is impossible for the infected population, for in 95 per cent of the cases gonorrhea is not bed-confining and few indeed are the patients who would jeopardize their jobs or risk the existing social dangers by entering an institution with an uncomplicated infection. There are fewer still who could bear the additional expenses of hospital confinement. However, we are in agreement with those physicians who recommend in-patient care if sulfanilamide only is given as the treatment of choice. We think that hospitalization is obligatory in these instances, for in this procedure lies the most complete safeguard for both the patient and the public.

Several writers have reported a high percentage of cures with sulfanilamide without adjuvant local therapy and have explained their failures as being due to a persistent or walled off lesion in the genital tract. We cannot square our experiences against these statements. Protracted localized infections of the urethral glands are infrequent and when present often produce painful or other subjective symptoms. A careful examination will usually disclose them. The fact is that sulfanilamide fails completely in a number of patients and we do not agree with the expressed opinion that when it does not benefit the patient it is due to a "locus minoris resistentiae". The reason why it fails completely in some patients is unquestionably due to unknown factors inherent in the human economy.

In previous communications we have reported our results in the treatment of gonorrhea in the male using sandalwood oil capsules by mouth and urethral injections of a mild solution of acriflavine. In a paper presented before the Neisserian Medical Society in June, 1936, we showed that in a group of 1,000 patients 37.5 per cent were discharged cured or non-infectious within twelve weeks, 16 per cent in sixteen weeks, 18 per cent in eighteen weeks, and 29 per cent were treated beyond this period. Compared with the two groups discussed above, we find that by administering twenty grains of sulfanilamide a day in place of sandalwood oil the percentage of cures obtained within twelve weeks is increased to 56 per cent, or a 20 per cent improvement; in eighteen weeks 34 per cent, or a 15 per cent gain, and from the eigh-

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teenth week onward a gain of 12 per cent.

The second group of 100 cases received forty grains of sulfanilamide daily with greater improvement and earlier cures. There were 82 per cent of the patients in this series discharged cured within twelve weeks. This was an improvement of more than 50 per cent over the patients receiving sandalwood oil capsules, and a 26 per cent increase over the group receiving twenty grains of sulfanilamide daily. The increase in dosage from twenty to forty grains daily doubled the number of reactions observed and disclosed that twice as many patients were allergic to the drug.

We are convinced that sulfanilamide, or its derivatives, will fill a therapeutic gap in the treatment of gonorrhea which has been missing since the birth of modern medicine. At the present time, however, we have not reached the stage where a true appraisal of the drug is possible. We are emerging from the period of unrestrained use and abuse when caution was disregarded and damage has been serious. We are approaching the stage where sanity is succeeding abuse and stability is being established. It requires about ten years for a new drug to have an established place in therapeutics and the mid-point in the use of sulfanilamide in the treatment of gonorrhea has not yet been reached. There is no question that the drug is useful and valuable but it will require time and further clinical experience to establish its true worth.

We will continue our conservative methods of administration of sulfanilamide in these infections as all of our patients are ambulatory, of the low income group, and in their various occupations they require all of the medical guidance, social protection and industrial safeguards with which we can surround them.

SUMMARY

1. A study of 200 cases of gonorrhea in the male treated with small and moderate sized doses of sulfanilamide and local injections of acriflavine is presented.

2. One-half of the group (100 patients) received twenty grains of sulfanilamide and anterior urethral injections of acriflavine daily and the other half (100 patients) received forty grains of sulfanilamide and anterior urethral injections of acriflavine.

3. An outline of the treatment procedures and tests of cure as followed in our clinic is given in detail. The tests required before discharge from treatment consume about six weeks.

4. Of the group of 100 cases which received twenty grains of sulfanilamide daily, ninety-two completed all tests of cure and eight became delinquent but were non-infectious. Of the total number 56 per cent were discharged cured in twelve weeks, and 31 per cent before the end of the twentieth week. The remainder were under treatment for varying periods of time. Details are given in a table.

5. The second group of 100 cases received forty grains of sulfanilamide and anterior injections of acriflavine daily. The treatment time was substantially shortened by doubling the amount of the medicament. In this series 82 per cent of the patients were discharged cured within twelve weeks and only 18 per cent were under treatment or observation for a longer period of time. Details are given in a table.

6. Of the 100 patients receiving twenty grains of sulfanilamide daily, 11 per cent were found sensitive to the drug and in half of these it had to be discontinued. Of the patients receiving forty grains of the medicament daily, 24 per cent showed an allergic response and ten of the cases could not tolerate it.

7. The results secured in these two groups of cases were superior to those obtained with any treatment methods heretofore available. With the small doses of twenty grains of sulfanilamide daily there is a 20 per cent improvement in twelve week cures and 15 per cent better results beyond this period. The patients receiving forty grains of sulfanilamide daily show a 50 per cent improvement in twelve week cures over older methods and 25 per cent better results over the group receiving twenty grains of the drug daily.

8. We think urethral injections are a necessary part of the treatment and especially in ambulatory patients. Mild antiseptic solutions used locally and given daily by the physician for the first two weeks aid in closer cooperation and secure better patient control.

9. The place sulfanilamide will occupy in the treatment of gonococcus infection in the male, especially in ambulant patients, must depend upon time and the unbiased sifting of divergent clinical experience and opinion.

159 North Dearborn Street.

EUGENIC STERILIZATION OF THE EPILEPTIC AND THE MENTALLY DEFICIENT.*

G. B. ARNOLD, M.D.,
Superintendent, State Colony for Epileptics and Feeble-Minded,
Colony, Virginia.

So far as I know, Kansas was the first of these United States in which eugenic sterilization operations without special therapeutic intent were performed on a large scale. The sterilization in a Kansas Home for the Feeble-minded of some sixty boys and girls, by castration and without authority of the law, so aroused public opinion that the practice was hastily abandoned.

From 1899 to 1907 some persons were eugenically sterilized, with their consent, in the State of Indiana. Then, in 1907, Indiana enacted a eugenic sterilization law and became the first State to sanction such surgical procedure by statute.

In 1909, California passed a well-written sterilization law; and it has pursued a rather vigorous policy of sterilization in its State Institutions ever since.

From year to year other states followed suit. Some of the laws were permitted to die from inertia, and some were found to be wholly unconstitutional. It seemed very difficult for the early legislators to view the matter of sterilization as anything but punishment; a mild sub-conscious sadism was exhibited by some of them.

In 1920 an attempt was made to enact an eugenic sterilization law in Virginia. It was never reported out of committee. Almost no interest was shown by the members of the Assembly. In 1922 a sterilization bill reached the floor, but it received almost no verbal support and only some few favorable votes. By 1924, however, the picture had changed radically, and the law passed both houses with hardly a dissenting vote!

The General Hospital Board decided that since similar laws in other states had been unable to survive Court action, it would be best to introduce a friendly suit to determine once and for all time the constitutionality of the Virginia statute. The State Hospitals and the State Colony agreed to share the expense of the litigation.

Dr. Priddy, who was then Superintendent of the State Colony, was asked to choose the patient for this "test case". He selected the now famous Carrie Buck. Carrie was a moron by almost anyone's standards. Her mother was even more feeble-minded. And to make the case just about perfect from the standpoint of the contestants, Carrie's illegitimate baby—then less than one year of age—had been pronounced definitely mentally deficient by several authorities.

Dr. Priddy, as provided for by the law, petitioned the Circuit Court of Amherst County to appoint a guardian to defend Carrie's interests in the sterilization proceedings. He then drew up a petition giving his reasons for believing sterilization justified. A copy of the petition, together with a notice as to the time and place of hearing thereof by the Special Board of Directors of the Colony, was then served upon Carrie, her mother, and Mr. R. G. Shelton, her guardian.

On the 10th of September, 1924, the Special Board of Directors assembled at the Colony. Carrie and her guardian appeared before the Board; all evidence in the case, both pro and con, was weighed carefully. After deliberation, the Board ordered that the Superintendent perform, or have performed by some competent surgeon, the operation of salpingectomy.

During the ensuing thirty-day period (which in every proceeding for sterilization in Virginia must elapse between the date of hearing and the date of operation) Mr. Shelton, as Carrie's guardian, appealed to the Circuit Court for a reversal of the action of the Special Board. This acted as an automatic "stay" in the proceedings.

The Circuit Court sustained the Board's contention that the rights of the patient had been safeguarded, that due process of law had been provided for, and the law was in no sense a cruel or unusual punishment.

From the Circuit Court the case was appealed to the Supreme Court of Appeals of Virginia; from there to the Supreme Court of the United States.

On the 2nd of May, 1927, Mr. Justice Holmes handed down the decision of the Supreme Court and said in part: "We have seen more than once that

*Read at the Post-Graduate Seminar of the Medical College of Virginia, during Spring, 1939.

the State may call upon the best of its citizens for their lives; it would be strange indeed if it could not call upon those who already sap the strength of the State, for these lesser sacrifices often not felt to be such by those concerned." And again: "The principle which sustains compulsory vaccination is broad enough to cover cutting of the Fallopian tubes." He also said, but not with strict accuracy, "Three generations of *imbeciles* are enough!" And to conclude with quotations from his opinion, "Of course, so far as the operations enable those who otherwise must be kept confined to be returned to the world and thus open the asylum to others the equity aimed at will be more nearly reached."

On the 19th of October, 1927, Carrie Buck became the first person ever to be eugenically sterilized in the State of Virginia under full authority of law.

The law provides that the Superintendents of the State Colony for Epileptics and Feeble-minded, the Eastern State Hospital, the Western State Hospital, the Central State Hospital, and the Southwestern State Hospital may perform, or cause to be performed by some capable physician or surgeon, after proper order by the State Hospital Board, a eugenic sterilization operation on any patient confined in such institution afflicted with hereditary forms of insanity that are recurrent, idiocy, imbecility, feeble-mindedness, or epilepsy.

The part played by heredity in the production of feeble-mindedness and epilepsy has been a much disputed point for years.

In 1935, Mr. John N. Buck, the Colony's Psychologist, searched the records of the 700-odd feeble-minded patients on the institution's books at that time. He found—and this, mind you, despite the fact that several hundred of the records were very scanty indeed—that 52 per cent of those patients had a definitely demonstrable positive heredity. And he was uncommonly conservative in the conclusions that he drew.

We cheerfully grant that many factors besides heredity play a part in the production of feeble-mindedness. But we well know that feeble-minded persons themselves all too often have children who are themselves mentally deficient, epileptic, or insane, and so far as I know there is no record anywhere of a really normal, intelligent child who was the offspring of a father and mother who were themselves mentally defective or diseased.

The part played by heredity in the production o epilepsy is by no means so clear-cut. In 1934 Mr. Buck searched the records of the 440-odd epileptics then on the institution's books. He found that abo 29 per cent had positive heredities, but that where 15 per cent of the feeble-minded had one or b parents feeble-minded, only 3 per cent of the ep tics had parents who were themselves epileptics, an in no case were both parents epileptics.

Our experience has been that if we know the county or city from which a patient comes, ir about 75 per cent of the cases we can state with certainty that the patient is related to one or more of three families in that city or county. Our opinion is that just about 5 per cent of the families in Virginia furnish some 90 per cent of the inmates of this State's mental and penal institutions! At times we are sorely tempted to support a proposition that all members of certain notoriously defective and diseased families in Virginia should be sterilized!

From all this, however, you must not draw the conclusion that we regard sterilization as a cure-all for mental deficiency or epilepsy, or that we regard the Colony simply as an institution whose main purpose is to admit patients, sterilize them, and return them to society in wholesale fashion.

But even though eugenic sterilization may perhaps still be open to debate if regarded solely on the grounds of inherited characteristics, certainly it cannot be questioned on economic grounds, for, even if the child of a feeble-minded or epileptic person did not, by some chance, inherit any of its parent's predeliction to mental disease or deficiency (which is most unlikely), that child's chances of reaching adulthood with a normal mind and normal personality would certainly be exceedingly slight.

It is well-known that many feeble-minded boys and girls, if sterilized, can adjust satisfactorily outside the institution and become at least partially self-supporting. Without sterilization, we should have to keep them in the Colony throughout the child-producing or child-bearing period of their lives.

The sterilization law provides for the sterilization of idiots; something for which we see no need. We also feel that it is senseless to sterilize markedly deteriorated and psychotic epileptics. The law also states that imbeciles may be sterilized, and we do operate upon a few who are sufficiently intelligent

id well behaved to be allowed to go home on occasional visits.

In our opinion, however, the logical candidates for rilization are those epileptics who have not deterated to any great extent and those feeble-minded and girls with mental ages ranging, say, from ten and a half or eleven years—all patients no, with a reasonable amount of training and supervision, should be absorbed into society without much ifficulty.

So much for the selection of patients. Now that e have chosen them, in what manner shall we sterilize them? The law specifies that vasectomy shall be performed upon the male; salpingectomy upon the female.

Vasectomy is a relatively simple operation. Perhaps a description of the operation as it is performed at the Colony will not be out of place here.

The scrotum is deadened with novocain; then the cord is located and held between the fingers. A small incision is made in the scrotum; the cord is delivered into the opening and a small section, perhaps a half of an inch in length is removed. The ends of the cord are then tied off and the cord is permitted to withdraw into the scrotum. The wound is then closed with one silk suture.

A slight infection occasionally follows, not as the result of carelessness on the part of the surgeon, but as the result of unbearable curiosity on the part of the patient who, on the night of the operation, must find out for himself whether his main source of pleasure has been destroyed.

The sterilization operation performed upon the female is a definitely major operation. In actual practice it might be termed salpingotomy rather than salpingectomy. The patient is anesthetized with avertin (which is later, if necessary, fortified with a small amount of ether, administered by drop method). A mid-line incision is then made. If the appendix has not already been removed, it is then taken out. Next any uterine pathology found is corrected. Following that, the tubes are resected at the uterine cornu and ligated, raw edges are covered with peritoneum, and the abdomen is closed by the layer method.

In neither the male nor the female is the individual's sexual life altered materially. Some few patients, usually women, have claimed that their sexual pleasure has been enhanced. This may be accounted for by the fact that the fear of pregnancy has been removed, though fear of pregnancy seldom deters women from illicit relationships. The men often claim increased libido (after all, however, vasectomy is the operation of rejuvenation for which many aged men of wealth have paid much and willingly).

In no case have we noticed any particular change in the individual's reaction to sexual matters. That is, the girl who was moral before operation usually remained so thereafter, and the girl who was immoral continued on the path of roses, if she was not closely supervised. This, of course, was to have been expected, since so far as I know no one has been able to bring about moral strengthening by surgery!

But all this is neither here nor there: sterilization has enabled us to release some 700 patients in the past twelve years on an indefinite basis. And several hundred more have been able to visit their homes periodically—all of this something that would have been out of the question if we had not had sterilization.

Sterilization has allowed us to permit our patients intra-mural liberties that would be out of the question without it. So even those who can never hope to leave the Colony for any length of time can find their lives somewhat more pleasant because of the law that was enacted in Richmond in 1924.

Thanks to sterilization, we need not resign ourselves to a policy of segregation only. And last, but by no means least, we have been able to develop an institution which has a healthy turnover and with which we can hope, as the years roll by and our educational program expands, to be of very real service to the unfortunate individuals in Virginia who suffer from epilepsy and feeble-mindedness.

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ECTOPIC PREGNANCY—A REPORT OF FIFTY-SIX PATIENTS.

RICHARD L. PEARSE, M.D.,
Durham, North Carolina.

Since Duke Hospital opened in 1930, fifty-six patients were treated for ectopic pregnancy up to February, 1939. Fifty-two patients were treated operatively and four were not. Of the fifty-two patients two had subsequent ectopic pregnancies treated at Duke Hospital by surgery, a total of fifty-four operative procedures. All of the pregnancies were tubal except one secondary abdominal pregnancy, one primary abdominal and two tubo-ovarian. One patient had chorionepithelioma of the tube; this patient has been previously reported in detail.[12]

Twenty-eight of the patients were white and twenty-eight were colored. The youngest was twenty years old and the eldest forty-one years. The incidence according to age was as follows:

20-24 years	15 patients	35-39 years	8 patients
25-29 years	20 patients	40-44 years	3 patients
30-34 years	10 patients		

Eleven of the patients were nulliparae, and forty-five were multiparae. The number of pregnancies preceding the ectopic gestation and the intervals were:

Para 1	7 patients	Para 6	6 patients
Para 2	5 patients	Para 8	2 patients
Para 3	15 patients	Para 9	1 patient
Para 4	3 patients	Para 11	1 patient
Para 5	5 patients		

Less than one year	7	10-14 years	3
1-4 years	16	15-19 years	1
5-9 years	8	Not recorded	10

The shortest interval between an intrauterine and an ectopic pregnancy was six and a half months; the longest was seventeen years. The shortest interval recorded by Scheffey[5] was four months. In all reported series multiparae have outnumbered nulliparae. Behney[4] feels that having borne children is no guarantee against ectopic pregnancy, but that the greater the number of intrauterine pregnancies the patient has had the less likely she is to have an extrauterine pregnancy. Scheffey,[5] on the other hand, feels that repeated pregnancy predisposes to ectopic pregnancy.

Six of the patients had previous appendectomies, seven dilatation and curettage, three appendectomy and a unilateral salpingo-oophorectomy, one an appendectomy and salpingectomy, one a salpingectomy, and one repair of an unbilical hernia and unilateral salpingo-oophorectomy. In none of the subsequent celiotomies were adhesions noted that might have occluded or twisted significantly the remaining tube.

All of the patients except two complained of some kind of lower abdominal pain. Thirty-six patients had a period of amenorrhea. This varied from a week to almost eight months in the case of a seven and one-half months' tubal pregnancy. On forty one occasions the onset of the pain definitely preceded the vaginal bleeding. On thirteen occasions the bleeding preceded the pain. Forty-four patients were bleeding on admission. The amount was usually scanty; the heaviest flow required two pads daily. Eight were not bleeding. On six occasions it was not stated whether vaginal bleeding was absent or present. Five patients had shoulder pain. In one case this was so severe that the patient could not be flat. Lewis and Carter[1] in studying a series of sixty cases found an incidence of 10 per cent.

Behney[4] has suggested that cases of ectopic pregnancy might be classified as obscure, urgent and non-urgent. Accordingly, the cases of this series might be divided as follows:

Obscure	8
Urgent	16
Non-urgent	34

In other words, ectopic pregnancy rarely presents the classical train of symptoms so graphically described in the older textbooks. In this series twelve patients were operated as emergencies. The remaining forty-two patients presented symptoms of such chronicity that a delay of from one to sixteen days elapsed before celiotomy was performed. The average delay before operation was about three days. The consensus appears to be that the mortality rate is lowered as the time elapsing between the onset of symptoms and operations is diminished.

Physical findings other than pelvic were not remarkable. Cullen's sign was seen once; it developed in a patient while she was under observation on the ward. A pelvic mass was present, either unilateral or in the cul-de-sac in forty-three patients, an in-

cidence of 75 per cent. Behney[4] reported the incidence of masses as 85 per cent and Tenney[8] 60 per cent. Thirty-one of the patients had fever. The elevations of temperature were from 37.4°C. to 39.6°C. A patient with malaria had the highest. The greatest elevation in an uncomplicated case was 38.7°C. The temperature was unrecorded for one patient who died promptly after admission. The remaining twenty-six had either a normal or slightly subnormal temperature.

Hemoglobin determinations on admission were as follows:

10-19 per cent--1 patient	60-69 per cent--14 patients
20-29 per cent--2 patients	70-79 per cent--12 patients
30-39 per cent--4 patients	80-89 per cent-- 6 patients
40-49 per cent--8 patients	90-100 per cent-- 2 patients
50-59 per cent--7 patients	

The highest recorded hemoglobin was 100 per cent and the lowest 14 per cent. The white count was recorded in fifty-four cases; twenty-four had a white count above 10,000. The highest was 26,000. Thirty had a white count of 10,000 or less, the lowest was 3,900. Sedimentation rate was reported in twenty-eight cases. The average was 17 mm. in thirty minutes. The most rapid was 30 mm. and the slowest 4 mm.

It has been generally accepted that the greater the hemorrhage into the peritoneal cavity, the more severe the general reaction. Acceleration of the sedimentation rate and leukocytosis are not so helpful in differentiating inflammatory disease from ectopic pregnancy. For example, a patient with a gestational sac almost 18 cm. in diameter completely enclosed by a pellicle of tube wall with almost no leakage of blood presented normal findings. Four Friedman's tests were performed. Only one was positive. A 4.0 cm. fetus had been extruded through a tubal rupture but the gestational sac was still in intimate contact with the tube. By the time most cases require hospitalization the sac has become detached with the formation of a tubal mole or abortion. One case with negative Friedman's test had a lipiodol injection in the course of sterility studies. The tubes both proved to be patent; the one containing the gestation was stretched, and the other kinked. No fetus was present and the tube was not ruptured at operation.

The recorded diagnosis preoperatively and before post-mortem examination was available in fifty-seven instances. Twenty-eight were correctly diagnosed by at least one person, an incidence of 48 per cent. Behney's[4] average of correct diagnoses was 61.3 per cent; Tenney's[8] 79 per cent; Grier's[11] 86 per cent; and Scheffey's[5] 78.7 per cent. The following variations in diagnoses occurred in fifty-three recorded instances. This number is the result of a number of members of the service giving an opinion of each case:

Salpingo oophoritis	12
Ovarian cyst	12
Pelvic abscess	4
Fibroid with infection	4
Fibroid	4
Pelvic cellulitis	3
Tuberculous peritonitis	3
Incomplete abortion	2
Hyperplasia of the endometrium	2
Pregnancy and myoma	1
Chronic subinvolution, post-partum	1
Reperitoneal hematoma	1
Prolapse	1
Ovarian mass	1

Fifty-six patients are included in this series. Fifty-two patients received operative treatment and two of these were operated twice, a total of fifty-four operations. One patient died post-operatively, a mortality rate of 1.8 per cent. Four patients were not given operative treatment; two of these died. The gross mortality was 5.3 per cent. Falk's[7] total mortality was 8.3 per cent and operative 6 per cent, Tenney's[8] was 4 per cent, Grier's[11] was 3 per cent, and Scheffey's[5] 4.8 per cent total, and 2.5 per cent operative. Hemorrhage was the cause of death in the unoperated cases and a combination of hemorrhage and sepsis in the operated case. Autopsies were performed on all patients.

I. E. T., a thirty-two-year-old, colored female, entered March 3, 1933, at 4:30 P. M.. She was para 2-0-2. She had been flowing three weeks, but had suffered from abdominal pain for only a few hours. Her temperature was 35.8°C. and blood pressure 80/60. Pelvic examination showed nothing except thickening and tenderness in the left vault. The patient was flowing. Her hemoglobin was 55 per cent and her white count was 10,000. She suddenly went into profound shock and died at 11:05 P. M. of the day of admission while receiving a transfusion. Post-mortem findings were a ruptured isthmic tubal pregnancy on the left. There were 800 cc. of blood in the peritoneal cavity. An 8.0 mm. fetus was in the gestation sac and the uterus contained decidua.

XUM

II. M. W., a twenty-five-year-old, colored female, entered Duke Hospital July 18, 1933. She was para 1-0-1. She had had amenorrhea for three months and thought herself normally pregnant. Six hours before admission she was seized with sudden lower abdominal pain and went into shock. No examination was made. She died four minutes after entry when an attempt was being made to give her gum acacia. Autopsy revealed a ruptured right tubal pregnancy. A gestation sac but no fetus was present; the tube was chronically inflamed. There was massive intra-abdominal hemorrhage. There was no decidua in the uterus.

III. M. W., a twenty-five-year-old, colored female, entered Duke Hospital, October 24, 1934. She was para 1-1-0. Her last period had been in July and she had missed the August period. She had an attack of lower abdominal pain and bleeding a month before entry and the symptoms had persisted. Her temperature was 35.8°C. and her blood pressure was 70-50. Physical examination in the admitting ward showed an enlarged uterus and a fluctuant mass in the cul-de-sac. The patient went into profound shock on her way to the ward. Her hemoglobin was 60 per cent and her white count 6,200. A transfusion was started. Under gas, oxygen and ether anesthesia an abdominal gestation about three months advanced was removed from the posterior surface of the right broad ligament. The tubes were not remarkable except for a few filmy adhesions. A pack was placed in the cul-de-sac for hemostasis. Her condition was poor. She was transfused on October 26. On October 28 she died; her pulse and temperature had risen steadily. Post-mortem examination showed chorionic villi in the cul-de-sac. There was considerable intra-abdominal hemorrhage. Both tubes showed healed salpingitis, and there was a decidual reaction in the uterus. The fetus removed at operation was 10.0 cm. long.

The operative procedure were as follows:

Removal of abdominal pregnancy, probably primary	1
Removal of abdominal pregnancy, secondary, and salpingo-oophorectomy	1
Unilateral salpingectomy	5
Bilateral salpingectomy	2
Unilateral salpingo-oophorectomy	16
Unilateral salpingo-oophorectomy with contra-lateral salpingectomy	10
Bilateral salpingo-oophorectomy	2
Supravaginal hysterectomy with bilateral removal of adnexa	7
Supravaginal hysterectomy with unilateral removal of adnexa	4
Total hysterectomy with bilateral removal of adnexa	4
Total hysterectomy with unilateral removal of adnexa	2

Colpotomy was performed nine times prior to celiotomy. In a vicinity where inflammatory disease is decidedly rampant this diagnostic procedure has proved very helpful. A digital exploration is preferable in doubtful cases to aspiration. No ill effects have been noticed following colpotomy. Twenty-four cases received transfusions, viz.:

7 before operation	1 during operation
9 after operation	7 before and after operation.

Associated procedures were:

Abdominal drainage	16	Myomectomy	1
Dilatation and curettage	4	Suspension	2
Appendectomy	10	Vaginal drainage	1

Most authors condemn drainage in cases of ectopic pregnancy. The peritoneum is better able to carry away the uninfected residuum if not insulted by a foreign body. It has even been recommended that the extravasated blood be left undisturbed in the peritoneal cavity. Gas, oxygen and ether were used forty-two times, novocaine spinal nine, straight ether three, and cyclopropane twice. Although no ill effects followed the use of spinal anesthesia it would hardly appear to be the anesthetic of choice because of the possibility of the great fluctuations of blood volume and blood pressure.

The post-operative complications were:

Minor wound sepsis	2
Shock	2
Pyelitis	1
Malaria	1
Secondary hemorrhage from the vagina following total hysterectomy	1

Two other cases of ectopic pregnancy were admitted to Duke Hospital. One was correctly diagnosed and operation advised. She left against advice and a letter from her physician reported an old gestation in the left tube. The other patient was treated from June 24, 1934, to July 5, 1934, with douches and non-specific foreign protein because of the mistaken diagnosis of salpingo-oophoritis. She had an operation subsequently elsewhere and a right ruptured tubal pregnancy was found.

In fifty-seven instances, according to operative, post-mortem and physical findings, the right tube was involved thirty-four times and the left twenty-three. The tubes showed only slight chronic inflam-

mation in the case of primary abdominal pregnancy. The other case of abdominal pregnancy was obviously secondary to tubal abortion, as the gestation sac was intimately connected with the right tube. There were two patients in whom no site of nidation was present in the tube and in whom villi were discovered in a clot adherent to the ovary. In one patient the tube was normal and in the other chronic inflammatory changes were present. Both were right-sided and in both the fimbriae were adherent to the clot. Presumably, these were tubo-ovarian pregnancies. One patient was treated in the out-patient department for three months with douches and non-specific foreign protein. The tubes were ruptured nineteen times, unruptured thirty-four times, intact twice and of unknown state three times. The portion of the tube in which nidation had occurred is as follows:

Proximal	3	Distal	25
Mid	1	Unknown or uncertain	28

According to Falk[7] the tube is usually ruptured. Most of the specimens in this series presented a greatly distended intact tube containing a degenerated gestational sac surrounded by blood. Clotted blood was being extruded from the fimbriated end. Most of the specimens could be classified as tubal moles or abortions. Fetuses were found in twelve cases, and macerated fetal parts in one case. They varied in size from 8.0 mm. to seven and one-half months. The patient who carried her tubal pregnancy to such an advanced state was a thirty-year-old, colored female, para 4-2-2. In June, 1931, she had an episode of flowing diagnosed by her doctor as an abortion. She had no subsequent menses. In July, 1931, she noticed abdominal enlargement and thought herself pregnant. In February, 1932, she had pain and flowed for thirty days. The abdominal tumor continued to enlarge. She entered the hospital on July 5, 1932, and presented a large lower abdominal tumor. It was fully 23.0 cm. in diameter and cystic. The uterus was enlarged and anterior. On July 7, 1932, a large right tubo-ovarian mass was removed under gas, oxygen and ether and the abdomen drained. The mass proved to be an intact tube containing a macerated seven and one-half months' fetus.

Endometrium was obtained by dilatation and curettage, hysterectomy or at post-mortem twenty-four times and once in the form of a decidual cast. A fetus was present on eight occasions, including the patient who passed a cast. The Friedman's test was positive also. In six there was a decidual reaction, and in two normal interval endometrium. On sixteen occasions no fetus was present. In two cases a decidual reaction was present, including the patient with chorionepithelioma of the tube. In the remaining fourteen patients normal interval endometrium was discovered. According to Kline,[2] there is usually some decidual formation in the tube at the actual site of nidation but the formation of sympathetic decidua is not constant. When it does occur it may persist after degeneration of the chorionic villi and disappearance of the local decidual reaction. Schuman,[3] on the other hand, believes that a sympathetic decidua is always produced *in utero*, and with the termination of the ectopic gestation is exfoliated as lochia. The relationship of the symptom of flowing to the status of the ectopic gestation is illustrated by the following table:

Fetus Present		No Fetus	
Decidua	Endometrium	Decidua	Endometrium
6	2	2 including chorion epithelioma of the tube	14
		Flowing	
5	1	1	12
		Not Flowing	
1	1	1	2

From this short series it is apparent that the bleeding can occur regardless of the histological picture of the endometrium and that none of the present theories explain the mechanism of how a patient can bleed from a fully developed decidua or from an apparently estrogenic endometrium.

Chronic inflammation of the tube occurred in twelve patients and acute inflammation once. One patient had a frank tuberculous salpingitis. Tubercle bacilli were demonstrated in the sections. A diverticulum of the tube was reported in one patient but the pregnancy was not in it. Other abnormalities discovered at operation were:

Fibromyomata	3
Endometriosis of the ovary	1
Acute appendicitis	1

The finding of an acute appendix was most unexpected and might be considered justification for a more extensive exploration than is usually carried out. Inflammatory changes, chronic, acute, or tuberculous occurred in 21 per cent of the patients of this series. Grier[11] reported an incidence of 17 per cent,

Miller[10] 20 per cent and Tenney[8] 25 per cent. In the face of all this it hardly seems advisable to dismiss inflammation as a possible etiological factor.

There were four patients in the series who had recurrent tubal pregnancies. Two had been operated elsewhere, and two had both gestations treated in Duke Hospital. This represents an incidence of about 7 per cent. Schuman[3] says that one woman in eight who has had an ectopic pregnancy may expect another ectopic, and one in four a normal pregnancy. Of Gregerssen's[6] ninety-five patients, four had had previous ectopic pregnancies. Holtz,[9] in a series of 111 operated patients, had nine develop fresh tubal pregnancies.

I. P. A., a thirty-one-year-old white, married female. No previous intra-uterine pregnancies. In December, 1937, a left salpingectomy and appendectomy were performed in Rocky Mount Sanitarium for tubal pregnancy. She missed no periods. About July 14, 1938, she had a severe lower abdominal pain and then commenced to flow. She had a mass in her right vault. Hemoglobin was 100 per cent, and white count 5,200. Sedimentation rate was 4 mm. in half an hour. On August 31, 1938, under cyclopropane and ether anesthesia a posterior colpotomy, partial right salpingectomy and total hysterectomy were performed. The tube was not ruptured. Villi were present. The convalescence was uneventful.

II. W. B., a thirty-seven-year-old, colored, married female. She was para 5-1-3. In 1934 the left tube had been removed in Goldsboro, N. C., for ectopic pregnancy. Her last pregnancy had terminated spontaneously at term sixteen months previously. Her previous period had been February 15, 1938; she had flowed five days. On March 9, 1938, she fainted. She commenced to flow March 14. She had a mass in the right vault. Temperature was 38.2°C., pulse 104, respirations 20, blood pressure 140/90, hemoglobin 35 per cent, white count 5,600, and sedimentation rate of 33 mm. in thirty minutes. She was given 500 cc. of citrated blood and on March 23, 1938, dilatation and curettage, left oophorectomy, right salpingo-oophorectomy and supravaginal hysterectomy were performed under gas, oxygen and ether anesthesia. The uterus contained a degenerating myoma. The right tube was ruptured and contained villi. The wall was infiltrated with leucocytes and lymphocytes. She had an attack of paroxysmal tachycardia, but otherwise her convalescence was uneventful.

III. P. A., a twenty-seven-year-old, white, married female, para 3-0-3. Her last pregnancy had terminated at term in 1935. Her previous period had been December 25, 1936. On January 29, 1937, she had cramps in her lower abdomen. On February 4, she commenced to flow. There was a mass 4.0 cm. in diameter in the left vault. Temperature, pulse and respirations were normal. Sedimentation rate was 6.0 mm. in thirty minutes. On February 27, 1937, a left salpingo-oophorectomy was done under gas, oxygen and ether anesthesia. There was a pregnancy in the ampullar portion with one small point of rupture and chronic inflammation was present in the wall. Her recovery was uneventful. She had normal menses subsequently. On March 10 she commenced to flow at the time of her expected period and continued. About March 17 she had pain in her right lower quadrant. She had a mass in the right vault. Temperature, pulse and respirations were again normal. Hemoglobin was 78 per cent, white count 6,000, and sedimentation rate was again slow, 5 mm. in thirty minutes. On April 5, 1938, under gas, oxygen and ether anesthesia a posterior colpotomy, right salpingo-oophorectomy, total hysterectomy and appendectomy were done. She was drained vaginally. The tube was not ruptured and was chronically inflamed. The cervix was large, boggy and infected. Again her convalescence was uneventful.

IV. A. H., a twenty-six-year-old, colored female, entered November 5, 1935. She was para 1-0-1. She had been flowing for a month and had very little pain. She had a large fluctuant mass in the right vault. A right oophorectomy and appendectomy had been performed elsewhere in 1932. On November 8, 1935, a right salpingectomy was done. The left adnexa were normal. The pathological report was "An intact tube containing a clot with chorionic villi visible. No inflammation." The patient had an uneventful recovery. She re-entered April 16, 1937. She denied having missed any periods but had she had commenced to flow April 2 and April 9, and had considerable lower abdominal pain. A mass was palpable in the left fornix. On April 21, 1937, a left salpingectomy was performed. This tube was intact, contained a small gestational sac without fetal elements, and was chronically inflamed. Her convalescence was uneventful.

In conclusion, it seems proper to refer to Behney's criteria for diagnosing ectopic gestation, viz., amenorrhea, recurring lower abdominal pain, metrorrhagia, signs of pregnancy and a pelvic mass. Also, anybody who has seen many ectopic pregnancies can subscribe to his statement that the average case does not conform to a typical picture.

The author thanks Drs. F. B. Carter and R. A. Ross, Duke University, Department of Obstetrics and Gynecology, on whose services the patients were studied.

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602 West Chapel Hill Street.

Correspondence

Reply to Dr. Peters' Criticism.

December 6, 1939.

TO THE EDITOR:

In the last issue of the MONTHLY Dr. Peters, Secretary of the Committee of Physicians for the Improvement of Medical Care, Inc., quoted this statement from an address made by me: "It is an interesting fact that not one of the 430 physicians resigned from the A.M.A.'s roster of 110,000 members."

Dr. Peters continued his letter by the following remarks:

"The speaker seems to imply that resignation is the only measure by which a minority in this organization can properly express its disapproval of the policies of the majority. He is not the first to air this opinion which seems to violate the first principle of democracy, the liberty of minorities to voice and to further their convictions."

The implied criticism of the Committee was that its members were inconsistent. Freedom of expression of opinion by minorities as well as other groups was open to them within the ranks of the A.M.A. where democratic principles dictated that differences of opinion should be freely discussed, matters of policy determined, and the will of the majority supported. If instead of playing the game according to the well-established rules of democracy, these men preferred to establish a separate organization outside of the A.M.A., it is still an interesting fact to me that not one of them resigned from the A.M.A. By exploding their bomb-shell of revolt in a carefully chosen Sunday Edition of the *New York Times*, they were in my opinion hitting below the belt. But of still greater importance they were unconsciously giving comfort to the enemies of independent medicine, and aiding and abetting those forces striving for the complete socialization of medicine.

The struggle of medicine, for its independence, on an isolated front, against tremendous odds, demands a unity of purpose and a harmony within our ranks which has been much nearer attainment in the past year. In the interest of both unity and harmony there is no point in prolonging this controversy.

ALEX F. ROBERTSON, JR.

Public Health Statistics

I. C. RIGGIN, M. D.
State Health Commissioner of Virginia

The report of the Bureau of Communicable Diseases of the State Department of Health for November, 1939, compared with the same month in 1938, follows:

	1939	*1938*
Typhoid and Paratyphoid Fever	23	23
Diphtheria	291	336
Scarlet Fever	227	195
Measles	29	75
Meningitis	5	4
Poliomyelitis	4	1
Rocky Mountain Spotted Fever	0	1
Typhus Fever	1	2
Undulant Fever	0	1
Tularemia	8	16

FINDING TUBERCULOSIS WITH THE X-RAY

Paper X-ray films have made wholesale chest X-rays possible and practical on large groups of individuals. Ingenious equipment, using the principle of the roll camera, makes it possible to examine six or seven hundred individuals a day at small cost. After processing, the films are returned in rolls of one hundred each, which then are interpreted on a special viewing box with direct lighting. Detail is not so good as on the celluloid film, but it permits the recognition and diagnosis of the earliest visible tuberculosis lesion. This method is not applicable for use in private office or X-ray laboratory, but it does offer for the first time an excellent method of locating unsuspected and unknown cases of tuberculosis with very little interruption or loss of time in industrial plants, schools, colleges and hospitals.

Tuberculosis ordinarily is not considered to be an occupational disease, but the national death rate among unskilled workers is more than twice that of the skilled trained workers. The State Health Department plans to incorporate much industrial work into its tuberculosis program during the coming year, and in this activity will use the paper films.

TULAREMIA INCIDENCE

The number of reported tularemia cases in 1939 was but slightly less than the total recorded by the State Department of Health for 1938. This is significant in view of the fact that the 1938 figures represented the highest incidence since this disease was added to the reportable list by the Department in 1928.

Aside from its presence, little actually is known about the extent or spread of this infection among the rabbits and other small wild animals of the Commonwealth, though it would appear that few sections are free from it. It, therefore, is necessary to consider all rabbits, other than the domestic variety, as potentially infectious.

Those who casually dress small game need to take more seriously than hitherto has been the case the advice given patients and the public by the medical profession and health officials.

Undoubtedly, the increase in reported cases in some measure can be explained by a keener observation and more accurate diagnosis on the part of the general practitioner. However, the necessity of continually educating the public on the exercising of care in handling the carcases of wild rabbits is apparent.

EXPANSION OF LABORATORIES

Due to the increased use of the Department's central laboratory facilities by physicians throughout the State, arrangements recently were completed in the State Office Building for additional laboratory space. A rearrangement of the equipment and provision for laboratory work in connection with the industrial hygiene program are expected more comfortably to maintain the various diagnostic and research services for which the laboratory is responsible.

Since the adoption of the Neufeld technic as a routine procedure, requests for pneumococcus typing have increased consistently. Specimens of sputum are now being examined by this method directly for the thirty types of pneumococci. The types in order of their predominance in Virginia during 1939 were: Type I, Type III, Type II, Type VII, Type X, and Types V, VII, XII, XIV, XIX, XXIII, XXV.

There also has been a definite expansion in the laboratory's media work. During the last twelve months the number of specimens submitted for examination for evidence of syphilis constituted 59 per cent of the total number of specimens received.

Woman's Auxiliary to the Medical Society of Virginia

President—MRS. HENRY A. LATANE, Alexandria.
President-Elect—MRS. GRIFFIN HOLLAND, Eastville.
Recording Secretary—MRS. T. N. HUNNICUTT, Newport News.
Treasurer—MRS. REUBEN F. SIMMS, Richmond.
Parliamentarian—MRS. JOSEPH BEAR, Richmond.
Chairman, Press and Publicity—MRS. HENRY M. SNEAD, Petersburg.

Norfolk Auxiliary.

The Woman's Auxiliary to the Norfolk County Medical Society held its November meeting at the home of Mrs. C. M. McCoy, on Wednesday morning, November 15, with Mrs. H. W. Rogers, president, presiding. Plans were made for the entertainment of wives of doctors who would attend the meeting of the Seaboard Medical Association at the Cavalier Hotel, Virginia Beach, on December 13 and 14. A luncheon, fashion show and tea were planned for the first day, and on the second day it was arranged to take the visitors on a sight-seeing tour of Norfolk and vicinity.

The Auxiliary set January 24th as the day for its annual card party, which will be held at the Town Club. This party is given every year to raise money to maintain a bed at the Tidewater Victory Memorial Hospital, but this year the proceeds will be used not only for this fund, but will be divided with the Diagnostic Tumor Control Clinic and other charitable organizations.

Mr. Donald Shriver spoke in behalf of the American Red Cross and its annual Roll Call, then in progress.

(MRS. BROCK D.) EUGENIA H. JONES,
Chairman, Press and Publicity.

Truth About Medicine

In addition to the articles previously enumerated, the following have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association:

Mead Johnson & Co.

Mead's Mineral Oil with Malt Syrup.

Parke, Davis & Co.

Vitamin K in Oil.

Capsules Viatmin K in Oil.

New and Nonofficial Remedies

The following products have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in New and Nonofficial Remedies:

Dilantin Sodium.—Sodium 5, 5-diphenyl-hydantoinate.—Sodium 2, 4-diketo-5, 5-diphenyl-tetrahydroglyoxaline.—The mono-sodium salt of 5, 5-diphenyl-hydantoin. Dilantin sodium is an anticonvulsant with a relatively weak hypnotic action. It is used in the treatment of epileptic patients who are not benefited by phenobarbital or bromides and those in whom these drugs induce disagreeable side actions. It appears to be more effective in controlling seizures of the grand mal type than in those of the petit mal. Various side actions of different degrees of severity have been observed. The product is marketed in the form of kapseals, 0.1 Gm. (1½ grains), and 0.03 Gm. (½ grain). Parke, Davis & Co., Detroit.

Tablets Suprarenin, 0.02 Gm.—Each tablet contains suprarenin bitartrate 0.0364 Gm., equivalent to suprarenin (New and Nonofficial Remedies, 1939, p. 232), 0.02 Gm., with lactose 0.0385 Gm., and acetone sodium bisulfite not more than 0.0001 Gm. Winthrop Chemical Co., Inc., New York. (*J. A. M. A.*, November 11, 1939, p. 1813.)

Typhoid-Paratyphoid Bacterial Vaccine Immunizing (New and Nonofficial Remedies, 1939, p. 443).—This product is also marketed in 50 cc. vials, twenty immunizing doses, containing in each cubic centimeter 1,000 million killed typhoid bacilli, 500 million killed paratyphoid A bacilli and 500 million killed paratyphoid B bacilli. The Gilliland Laboratories, Inc., Marietta, Pa.

Propaganda for Reform

Chorionic Gonadotropin.—The Council on Pharmacy and Chemistry reports that the numerous names which have been given to the gonadotropic substance excreted in the urine of pregnant women have led to considerable confusion and ambiguity for many years. Investigators have commonly referred to this urinary gonadotrope as the anterior pituitary-like substance. Other names by which this substance is known are P. U., A. P. L., pregnancy urine hormone and prolan B. Fluhmann suggested in 1934 the name "Chorionic ovary-stimulating hormone," since it was definitely shown that this substance was elaborated by chorionic tissue, such as the placenta, hydatid mole, chorio-epithelioma and certain embryonal teratomas. In 1937 the Council voted to adopt as the designation of this substance the term "chorionic gonadotropin," which signifies its origin from chorionic tissue and its gonadotropic action. This action was not published at that time. At the League of Nations Third International Conference on the Standardization of Hormones in 1938 it was agreed to adopt "the term 'gonadotrop(h)in' for reference to principles with gonadotrophic action, with the addition, in each case, of a suitable adjective or descriptive phrase, to indicate the source of origin of the particular principle to which reference is made." This is in close agreement with the action of the Council, and it appears, therefore, that the term "chorionic gonadotropin" is an international one. (*J. A. M. A.*, August 26, 1939, p. 756.)

Book Announcements

Manual of the Diseases of the Eye. For Students and General Practitioners. By CHARLES H. MAY, M.D., Consulting Ophthalmologist to Bellevue, Mt. Sinai and French Hospitals, New York; formerly Chief of Clinic and Instructor in Ophthalmology, Medical Department of Columbia University, etc. Sixteenth Edition, Revised with the Assistance of CHARLES A. PERERA, M.D., Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department of Columbia University, New York. Baltimore. William Wood and Company. 1939. 515 pages, with 387 illustrations, including 31 plates, and 95 colored figures. Cloth. Price $4.00.

Considering the voluminous material in books and magazines, appearing every month, it is quite impossible for a prodigious reader to devote enough time to read and digest all the material. It would be impossible for such a small volume to contain all the details of the special eye work going on throughout the world.

Dr. May has very skillfully extracted the important new advances in the growing field and combined them with the brief essentials truly needed by every physician. (Each subject is of informative value, but necessarily so brief that the interested reader will have to search further if he wishes a comprehensive understanding of the matter.)

The chapter on perforating wounds and compensation for eye injuries is one of common sense and everyday practical value to every physician. It is concise and I strongly advise everyone to read this chapter.

The chapters on glaucoma, visual standards, disturbances of mobility and ocular therapeutics, have included the most recent scientific advances. Many of the chapters had been revised and many new plates added. This revised edition well accomplishes its original purpose of presenting a concise and practical foundation of ophthalmological knowledge for the undergraduate student and general practitioner.

This book has had fifteen editions and has been translated in eight foreign languages and speaks for itself.

L. B. SHEPPARD.

Pneumonia and Serum Therapy. By FREDERICK T. LORD, M.D., Clinical Professor of Medicine, Emeritus, Harvard Medical School; Member of the Board of Consultation, Massachusetts General Hospital; and Member of Massachusetts Advisory Committee on Pneumonia, 1931-5. And RODERICK HEFFRON, M.D., Field Director, Pneumonia Study and Service, Massachusetts Department of Public Health, 1931-5. Revised Edition of Lobar Pneumonia and Serum Therapy. New York. The Commonwealth Fund. 1938. 153 pages. Cloth. Price $1.00.

This book in some respects is a brief for the use of anti-pneumococcic serum in the treatment of certain types of pneumonia. The statistics used to prove this contention were collected from an analysis of data relative to the work done by the Massachusetts commission for the study of pneumonia from the years 1931 to 1936, inclusive. This work, as is generally known, was initiated by Dr. George H. Bigelow and financed by the Commonwealth Fund.

The various phases of pneumonia are discussed briefly, but satisfactorily. Some space is given to the differential diagnosis of lobar and bronchial pneumonia, but more emphasis is placed on the fact that, while the clinical course of each may be entirely different, the causative organism in either may be a type of pneumococcus for which a specific serum is available. In other words, the present-day concept is that the differentiation between lobar and bronchial pneumonia on clinical or anatomical grounds, or both, is not enough, and that both types should, in addition, be studied from the bacteriological standpoint. The various steps from the collection of sputum to the technique of the various methods for typing the pneumococci are given.

Needless to say this is a report of the most extensive experiment of its kind ever undertaken. The data come not only from the medical center of Massachusetts, but from the general practitioners as well throughout the state, and as mentioned before covers a period of five years. The data are analyzed from every conceivable standpoint as, for example, the effects of early and late administration of serum, dose, factors responsible for failures, complications, etc. Statistically the authors prove their case.

In conclusion, one has only to read such a book as this to realize the superior worth of research of this kind as compared with that in which the scope is extremely narrowed. The analysis of this study not only shows the value of serum, but also the obstacles which must be overcome in order that its use may have wide practical application. In addition, it shows what may be expected if such a thing could be done under circumstances in which the average doctor practices medicine. The authors concluded that, in order for all patients to get the maximum benefit to be derived from this therapy, it will be

necessary not only to have physicians who understand the problem, but technicians and laboratory equipment generally available for aid in diagnosis; and, what is almost of equal importance, adequate financial aid to make serum available to all.

HARRY WALKER.

Diagnostic Signs, Reflexes and Syndromes. Standardized by WM. EGBERT ROBERTSON, M.D., F.A.C.P., Visiting Physician, Medical Division, Philadelphia General Hospital, St. Luke's and Children's Hospital, and Northeastern Hospital. And HAROLD F. ROBERTSON, B.S., M.D., F.A.C.P., Instructor in Medicine, University of Pennsylvania; Assistant Visiting Physician, Medical Division, Philadelphia General Hospital and Methodist Hospital. Philadelphia. F. A. Davis Company. 1939. 12mo of ix-309 pages. Imitation leather. Price, $3.50.

The purposes of this book, as stated in the publisher's foreword, are: 1. to provide easy reference to the signs, reflexes and syndromes useful in diagnosis; 2. to trace back and check the first and authoritative description of each such item; and 3. to standardize the nomenclature which is often confused and conflicting. These purposes are laudable and if the data are well assembled should make a very useful book.

The signs, reflexes and syndromes are arranged in alphabetical order, as in a dictionary, and included in this same alphabet are numerous pathological conditions, fields of medicine and diagnostic procedures to which the signs apply. Naturally in such an arrangement, any particular sign is liable to appear in more than one place and so cause undesirable duplication. For example, Baron's sign is found under Baron and under appendicitis, each entry occupying about twenty lines. Acroasphyxia and Raynaud's sign have exactly the same text under both terms using about twenty lines in each case. Under hemiplegia there are four pages of signs, nearly all of which are duplicated elsewhere. The same is true of tuberculosis with two pages and appendicitis with nine pages.

Distribution of the material also seems to be very uneven. For example, appendicitis has nine pages of signs while peritonitis has only four signs. Twenty-five signs are listed under hyperthyroidism, none under hypothyroidism, cretinism or myxedema.

A much more liberal use of cross references would have made a more useful book; for example, the cardiovascular system covers two pages but there is no such entry as circulatory system. Gastroenterology covers two pages but there is no such entry as digestive system. Nervous and mental diseases cover four pages but there is no such entry as nervous system, neurology or psychiatry. Typhoid fever has a whole page, typhus fever nothing. Ear, nose and throat has a page of signs and otorhinolaryngology, strangely enough, a page of reflexes.

There is no entry for anus, proctology or rectum, nor for dengue, psitticosis or tularemia, nor for heart block, auricular flutter of coronary thrombosis and malaria, angina pectoris and skin diseases have just one each.

If one looks up Richet and Netter's sign, one reads "See contraction of adductors sign"; here one reads "See under appendicitis"; here one reads "See adductor reflex" and here at last one finds a full page description of this sign as a reward for perseverance.

The next edition offers a wonderful opportunity for improvement.

E.C.L.M.

Nutrition and Diet in Health and Disease. By JAMES S. McLESTER, M.D., Professor of Medicine, University of Alabama. Third Edition, Entirely Rewritten. W. B. Saunders Company. Philadelphia. 1939. Octavo of 838 pages. Cloth. Price, $8.00.

This book contains a brief review of the metabolism of food vitamins and minerals. It also discusses various food products such as milk, meat, eggs, etc. in respect to their hygienic standards, nutritional value, vitamin content, digestion, etc. A long list of menus for a normal diet of infants and adults is given as well as special diets in disease, as deficiency diseases, diabetes, gout, obesity, allergy, renal diseases, digestive disorders, febrile conditions, and post-operative convalescence.

The appendix lists the mineral and vitamin contents of foods.

This is an excellent book which seems complete enough to cover the needs of the practicing physician who does not have the advantage of a department of dietetics to assist him. The reviewer would offer as criticism the minor suggestion that Doctor McLester's modifications of the Sippy diet does not afford the patient any source of vitamin C for a period of two weeks. This seems to be too long a time for a sick person to be without this vitamin which is not easily stored by the body.

R.J.M.

XUM

Virginia Medical Monthly

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Editorial

Another Committee.

Many doctors in the United States were asked a few days ago to join a committee formed, with the knowledge and consent of the A.M.A., to guide national legislation into channels that will give more and better medicine to our people, and to protest and oppose further encroachments upon the profession as it exists today by advocates of socialized medicine. Obviously the committee is designed to offer counter propaganda to the propaganda of the Committee of 430. It proposes to speak for the profession at large and not for a group of a few hundred. It is formed within the ranks of the membership of the A.M.A. and proposes to work with and through that organization. It will employ the channels doctors are accustomed to use in communicating their ideas to each other—the mails, medical journals, and official publications. It does not propose to plead its case in the public press, nor before a minority of the American people, a minority which has given evidence of a willingness to destroy the traditional position of the medical profession, if not to make a Roman holiday, to continue a social experiment whose ideology based on the worthlessness, not the worth of the individual.

Belladonna a la Bulgaria.

The introduction of a new pharmaceutical preparation first successfully tried in Bulgaria is deserving of mention. R. Finley Gayle, Jr., professor of neuropsychiatry at the Medical College of Virginia, reported it in the last issue of the VIRGINIA MEDICAL MONTHLY. The preparation is marketed under the name of Rabellon and contains hyoscyamine hydrobromide, atropine sulphate, and scopolamine hydrobromide. It is an extract of the root rather than of the leaf of the belladonna plant. It appears to have greater potency and less toxicity than the drugs we have been using. With doses of from two to five mgm. more satisfactory results are obtained than with much larger doses of the alkaloids, atropine or scopolamine. Dryness of the mouth, dilatation of the pupils, gastrointestinal symptoms and megalocolon are not encountered. The systematic improvement in muscle spasticity and tremor as well as in mental symptoms which patients exhibit after its use is described as dramatic. There is still much to be desired in the way of experimental proof of the mechanism of the pharmaceutical action of the preparation, but concerning its clinical effectiveness there seems to be a unanimity of favorable opinion. With liver preparations, with cod liver oil preparations and with some drugs we have learned that the crude substances often exceed the more refined substances in therapeutic effectiveness, and there has been a return to many of them on the part of the profession. This preparation of the root of belladonna may represent an example of a similar situation.

A Triad of Specifics.

To sulfanilamide and sulfapyridine a third drug has been added—sulfamethylthiazol. The last named is said to be surprisingly effective in staphylococcus aureus infections. Thus against the hemolytic streptococcus, the pneumococcus and the staphylococcus we now have drugs of great promise. Sulfamethylthiazol, as the name implies, is another sulfamido compound. It appears not to cause toxic manifestations as do the other derivatives, and yet it possesses equal if not greater bacteriostatic influence. Clinical reports are beginning to come through which indicate that it is not only effective in staphylococcus aureus sepsis, but also in pneumococcus pneumonia where its chief employment may be in those cases in which sulfapyridine cannot be given on account of nausea, vomiting and fear of calculus.

Sulfamethylthiazol is given in two gram doses every four hours for the first eight hours and thereafter in one gram doses every four hours as long as necessary. The blood concentration of the drug should be followed as in the case of the other members of this triad of specifics.

Rats!

Any temptation to treat lightly Rolland J. Main's little book, *The Care of a Small Rat Colony* (C. V. Mosby Company, St. Louis), is quickly dispelled by a reading of the text. In ninety-odd pages the author has compressed quantities of valuable information gathered in years of experience with one of science's humblest aids. Here may be found a great deal about equipment, cleaning, breeding, feeding and financing as well as remarks on the diseases to which rats are heir. To raise rats one must apparently combine talents for engineering, eugenics, nutrition, high finance and veterinary medicine. If all this is necessary one wonders how rats have managed to play the large and sinister role in human history that is sometimes credited to them. Perhaps the book could serve as a text for the professional exterminator who would make a success of his job by seeing to it that this pesky rodent was systematically denied all the favorable circumstances detailed in the book. Speaking seriously, we believe Dr. Main's book is useful, timely and entertaining.

Dr. Vinson's Book.

We have before us the *Diagnosis and Treatment of Diseases of the Esophagus* by Porter P. Vinson (Charles C. Thomas, Baltimore). It is a neat monograph of two hundred profusely illustrated pages dedicated to Henry S. Plummer, and covers the field from esophagoscopy to gastroscopy in a clear and comprehensive manner. Chapters on malignant and benign tumors, stricture, spasm, diverticula, injury, foreign body, acute and chronic inflammation, functional and extra-esophageal dysphagia follow one another in logical sequence.

The style is easy and there is an obvious avoidance of details of technique. The internist or general practitioner is made to feel that the subject is one in which he has a right to be interested and one in which he has the distinct responsibility of himself making an accurate and correct diagnosis in the great majority of cases. Emphasis is laid on the importance of a complete medical survey as a preliminary to detailed investigation of the esophagus. We are told that in 90 per cent of the cases a proper diagnosis may be reached by the history alone.

We expected to find a specialist in esophageal diagnosis and treatment approaching his subject with a pen in one hand and an esophagoscope in the other. It is a pleasant surprise to discover that Dr. Vinson regards himself as an internist primarily and that he only becomes an endoscopist when the occasion demands.

More from His Pen.

Primer of Allergy, "a guidebook for those who must find their way through the mazes of this strange and tantalizing state," by Warren T. Vaughan, (C. V. Mosby Company, St. Louis, 1939), is an echo of the author's larger and more technical volume, *The Practice of Allergy.* As far as size is concerned it is but a chip off that block. It is a handbook for the patient. The author hopes that it will prove "a reasonably good bed-time story." It is brief, nontechnical, pictorial, and, carrying out the figure that the fight against allergy is a war, allergens, sensitization, history taking, treatment, instructions and results are discussed in chapters bearing apt military sounding headings such as: "The Enemy," "Defense of the Realm," "Liaison and Reconnaissance," "Plan of Attack," "War of Attrition," "Victory or Defeat," "General Orders". The lay reader should enjoy this simple and clear presentation of a subject which is more and more commonly discussed. The last chapter dealing with directions to the patient will be found particularly valuable.

XUM

Proceedings of Societies

Southside Virginia Medical Association.

The regular quarterly meeting of the Association was held in Petersburg, December 12, with Dr. C. S. Dodd, president, presiding. Several Richmond doctors presented the following papers which were freely discussed: Dr. Thomas Wheeldon, "The Use of the Smith-Petersen Nail in Fractures of the Neck of the Femur"; Dr. James M. Whitfield, Jr., "Care of the Skin in a Newborn"; Dr. H. Hudnall Ware, Jr., "Complications Resultings from the Use of Sulfapyridine". Dr. Douglas G. Chapman, also of Richmond, then presented a series of motion picture films showing the action of the heart in certain abnormal conditions.

At the close of the Scientific session the business meeting was held. It was the general feeling of the members present that since the territory of the Fourth District Society and that of the Southside Virginia Medical Association was so nearly the same and since practically the same membership belonged to each society, it was best to combine the two in one medical association. Consequently, on a motion by Dr. C. S. Dodd, seconded by Dr. Wright Clarkson, and carried by the Association, such action was decided on. Drs. C. S. Dodd, Wright Clarkson and R. L. Raiford, secretary for many years, were appointed as a committee with a similar committee of the Fourth District Society to decide on the name for the new Society and make all necessary arrangements for the combination of the two.

The meeting then adjourned, closing the career of a long and useful service to the physicians of Southside Virginia.

Lynchburg Academy of Medicine.

The regular meeting of the Academy was held November 6, with the President, Dr. S. E. Oglesby, presiding.

Drs. William Jordan, Chief of the Diabetic Clinic and Harry Warthen, Associate Professor of Surgery from the Medical College of Virginia, presented a very complete and informative discussion on "The Medical and Surgical Aspects of the Elderly Diabetic." This very educational paper was thoroughly enjoyed by the members, many asking questions and entering into the discussion.

Dr. E. A. Harper, reporting for delegates to the State Medical Convention, states the resolutions submitted by the Lynchburg Academy of Medicine, in regard to some form of prepaid sick insurance for the low income group, were adopted by the House of Delegates.

The December meeting of the Academy was held on the 4th, with Dr. Oglesby, presiding.

This meeting was devoted entirely to business with reports of all of the committees and election of Dr. O. M. Weaver, State Colony, to membership.

Dr. E. G. Scott was elected president and Dr. Powell Dillard, vice-president. Drs. John Hundley, Jr. and Edwin Harper were elected to the Board of Trustees for two years, replacing Drs. Gorman and Devine, Sr.

C. E. KEEFER, M.D.,
Secretary-Treasurer.

Danville-Pittsylvania Academy of Medicine.

At the meeting of the Academy on December 12, the following officers were installed for the coming year: President, Dr. W. B. Sager; vice-presidents, Drs. M. H. Watson and W. E. Jennings; secretary-treasurer, Dr. E. E. Barksdale.

Richmond Academy of Medicine.

At the annual meeting of the Academy on December 12, the following officers were elected for 1940: President, Dr. J. Powell Williams; president-elect, Dr. William B. Porter; and vice-presidents, Drs. E. H. Terrell and H. J. Warthen. Drs. James P. Baker, Jr., and Ennion S. Williams were elected to the Board of Trustees. Following the business session, the annual Christmas party was held.

The Roanoke Academy of Medicine

Held its regular meeting on December 4, at which time the following scientific program was presented: A Report of Three Cases of Ethmoiditis with Unusual Complications by Dr. Mortimer H. Williams; Adenocarcinoma of the Pancreas with Metastasis to the Lungs by Dr. B. P. Seward; and Rocky Mountain Spotted Fever by Dr. J. H. Bailey.

Dr. L. G. Richards is president of the Academy and Dr. David B. Stuart, secretary-treasurer.

The Fredericksburg Medical Society,

At its annual meeting in December, elected the following officers for 1940: President, Dr. L. Philip Cox; vice-president, Dr. L. F. Lee; and secretary-treasurer, Dr. William Butzner, Jr.

The South Piedmont Medical Society

Held its regular meeting on November 28, in Danville, with the president, Dr. E. G. Scott, Lynchburg, presiding. The subject "The More Common Diseases of the Kidney and Bladder" was presented by Drs. Harold L. Riley, Lynchburg; W. Lloyd Eastlack, South Boston; and W. W. Koontz, Lynchburg. The general discussion was opened by Dr. W. M. Coppridge, invited guest, Durham, N. C. Following this discussion, papers were presented by Drs. Samuel Newman, Danville; Thomas Wheeldon, Richmond; I. C. Riggin, Richmond; Ray A. Moore, Hampden-Sydney; J. W. Devine, Sr. and Jr., Lynchburg; John Saunders, Madison Heights; S. C. Hall, Danville; Wright Clarkson, Petersburg; and J. J. Neal, Danville.

Dr. George A. Stover, South Boston, is secretary-treasurer of this Society.

News Notes

A NEW YEAR WISH

A happy heart, a smiling face,
A sunbeam in the darkest place.
A road to travel that is free
From ruts, and smooth and fair to see.
A bright objective, that will seem
To realize your fondest dream.
This may the New Year hold for you—
—*Selected.*

Southern Medical Association.

Dr. Walter E. Vest, Huntington, W. Va., president, presided at the thirty-third annual session of this Association in Memphis, Tenn., the latter part of November. The registered attendance was 4,082, of which 2,180 were physicians. There were the usual sectional, alumni and fraternity meetings and dinners, in addition to sports for those interested. In the scientific exhibits, that of Drs. W. W. Waddell, Jr., DuPont Guerry, III, and McLemore Birdsong, of the University of Virginia Department of Medicine, was among those to receive honorable mention.

Louisville, Ky., was selected as the 1940 place of meeting, under the presidency of Dr. Arthur T. McCormack of that city. Dr. Quitman U. Newell of St. Louis was named president-elect; Drs. W. L. Williamson of Memphis and E. W. Bertner of Houston, Tex., vice-presidents; and Mr. C. P. Loranz of Birmingham was re-elected secretary-manager.

The following physicians from Virginia were registered at this meeting:

Dr. Vincent W. Archer, Charlottesville.
Dr. J. B. Bailey, Keysville.
Dr. T. Neill Barnett, Richmond.
Dr. Ralph G. Beachley, Arlington.
Dr. I. A. Bigger, Richmond.
Dr. McLemore Birdsong, Charlottesville.
Dr. H. G. Bland, Newport News.
Dr. P. M. Chichester, Richmond.
Dr. Wright Clarkson, Petersburg.
Dr. Chas. E. Conrad, Harrisonburg.
Dr. V. M. Cox, Bristol.
Dr. Frank D. Daniel, Charlottesville.
Dr. J. H. Deyerle, Harrisonburg.
Dr. A. I. Dodson, Richmond.
Dr. Hunter M. Doles, Norfolk.
Dr. E. C. Drash, Charlottesville.
Dr. Granville Eastham, Culpeper.
Dr. Richard W. Fowlkes, Richmond.
Dr. H. B. Haag, Richmond.
Dr. Edgar C. Harper, Richmond.
Dr. Chas. L. Harshbarger, Norton.
Dr. J. S. Horsley, Richmond.
Dr. Robert Jones, Dorchester.
Dr. Linwood D. Keyser, Roanoke.
Dr. Walter B. Martin, Norfolk.
Dr. Howard R. Masters, Richmond.
Dr. G. M. Maxwell, Roanoke.
Dr. L. D. Morgan, Gladys.
Dr. T. Addison Morgan, Franklin.
Dr. H. B. Mulholland, Charlottesville.
Dr. Thos. W. Murrell, Richmond.
Dr. W. P. McDowell, Norfolk.
Dr. W. Ambrose McGee, Richmond.
Dr. J. B. Porterfield, Richmond.
Dr. Frank H. Redwood, Norfolk.
Dr. L. J. Roper, Richmond.
Dr. Jas. Warren Sayre, Hampton.
Dr. J. M. Shackelford, Martinsville.
Dr. James T. Shelburne, Critz.
Dr. Reuben F. Simms, Richmond.
Dr. James B. Stone, Richmond.
Dr. Landon E. Stubbs, Newport News.
Dr. Lee E. Sutton, Richmond.

Dr. E. H. Terrell, Richmond.
Dr. G. Colbert Tyler, Newport News.
Dr. Samuel A. Vest, Charlottesville.
Dr. W. W. Waddell, Jr., Charlottesville.
Dr. Thomas Wheeldon, Richmond.
Dr. David C. Wilson, Charlottesville.
Dr. J. Edwin Wood, Jr., Charlottesville.

The Seaboard Medical Association of Virginia and North Carolina

Held its forty-fourth annual meeting at Virginia Beach, December 12-14, under the presidency of Dr. Julian L. Rawls, of Norfolk. There were approximately 200 doctors present. Included on the program were symposiums on Sulfapyridine and Fractures.

The following officers were elected: President, Dr. John C. Tayloe, Washington, N. C.; vice-presidents, Drs. George A. Duncan, Norfolk; Erik G. Bell, Wilson, N. C.; Robert Matthews, Norfolk; and Winston Ruffin, Pink Hill, N. C.; and secretary-treasurer, Dr. Clarence Porter Jones (re-elected), Newport News. The next meeting will be held in Washington, N. C., December, 1940.

Medical College of Virginia News.

The portrait of Dr. A. L. Gray, late professor of roentgenology at the college, was presented to the college on December 15, with appropriate exercises in the Richmond Academy of Medicine auditorium. Mrs. Malcolm W. Perkins, a niece of Doctor Gray presented the portrait, painted by David Silvette, Richmond artist. Dr. Thomas W. Murrell and Dr. Lowndes Peple were the speakers on this occasion.

Founders' Day exercises and the dedication of the restored Egyptian Building will be held January 16, beginning with a morning program at Monumental Episcopal Church with addresses by Dr. Walter H. Judd and Dr. Wyndham B. Blanton. Dr. Judd is a distinguished student of Chinese culture and will speak on Chinese Medicine. Dr. Blanton will speak on the history of the Egyptian Building and its unique part in medicine in the South. Following this program the Egyptian Building will be inspected. At four o'clock in the afternoon the Brown-Sequard Society will present Dr. George W. Thorn, associate professor of medicine, Johns Hopkins University, school of medicine, who will speak on Studies on the Adrenal Cortex. This lecture will take place in the new Simon Baruch Auditorium in the restored Egyptian Building. In the evening at 8:30 o'clock the educational section of the Richmond Academy of Medicine will present in its auditorium, Dr. E. V. McCollom, professor of biochemistry, Johns Hopkins University, school of hygiene and public health, who will speak on The Place of Vitamins in the Maintenance of Normal Health. Members of the profession are cordially invited to be present for Founders' Day.

The annual Stuart McGuire Lectures are scheduled for April 16 and 17, with which the spring postgraduate clinics will be combined. Dr. Frederic C. Fluhmann, associate professor of obstetrics and gynecology at Leland-Stanford University, will give the lectures, the first on Anaesthesia and Analgesia in Obstetrics and the second on The Problem of Abnormal Uterine Bleeding. The spring postgraduate clinics will be held during the day of April 17 and will be devoted to the Toxemias of Pregnancy. Speakers will be Dr. N. J. Eastman, professor of obstetrics, Johns Hopkins University, school of medicine; Dr. Louis Douglas, professor of obstetrics, University of Maryland, school of medicine; Dr. Tiffany J. Williams, professor of obstetrics, University of Virginia, department of medicine, and Dr. Bayard Carter, professor of obstetrics, Duke University, school of medicine. The morning session will be from ten to twelve o'clock and the afternoon session from two to five o'clock. There will be a round-table discussion at the conclusion of the clinics. The ex-internes of the hospital division of the college will hold their annual reunion during the lecture period.

News from University of Virginia, Department of Medicine.

At the meeting of the Southern Medical Association in Memphis, Tenn., November 21 to 24, the following papers were presented by members of the Faculty of the Department of Medicine of the University of Virginia: Clinical Course and Management of Acute Nephritis by Drs. J. Edwin Wood, Jr. and Byrd S. Leavell; The Relationship of Personality Changes to Facial Neuralgia by Drs. Marion S. Love and David C. Wilson; and Roentgenologic Aid in Acute Infections of the Lung and Their Sequelae by Dr. Henry B. Mulholland. Drs. E. C. Drash and V. W. Archer participated in the discussions of several papers. Scientific exhibits were presented by Drs. John Eager Howard and Samuel A. Vest, Jr. on Administration of Synthetic Androgens by Pellet

Implantation and Pellet Injection and by Drs. W. W. Waddell, Jr. and DuPont Guerry, III on The Role of Vitamin K in the Etiology, Prevention and Treatment of Hypoprothrombinemia and Hemorrhage in the Newly-Born. Drs. Waddell and Guerry were awarded honorable mention for their exhibit.

Dr. Vincent W. Archer was elected Chairman of the Council of the Southern Medical Association.

Dr. David C. Wilson was elected Vice-Chairman of the Section on Neurology and Psychiatry. Dr. Wilson is also Chairman of the Section on Convulsive Disorders of the American Psychiatric Association and a member of the Committee on Research of the American Psychiatric Association.

On November 18, Dr. C. C. Speidel presented a paper before the American Philosophical Society in Philadelphia on The Effects of Metrazol on Tissues of Frog Tadpoles With Special Reference to the Injury and Recovery of Individual Nerve Fibers.

At the meeting of the University of Virginia Medical Society on November 27, Drs. E. P. Lehman and Floyd Boys discussed The Control of Intraperitoneal Adhesions with Heparin.

Drs. E. P. Lehman and Floyd Boys attended the meeting of the Southern Surgical Society in Augusta, Georgia, on December 6 and presented a paper on The Control of Intraperitoneal Adhesions with Heparin.

The sixth annual Postgraduate Course in Ophthalmology and Otolaryngology sponsored by the University of Virginia was held at the Medical School from December 5 to 8. The list of those giving lectures and holding clinics included the following: Dr. Edmund B. Spaeth, Associate Professor of Ophthalmology of the Graduate School of Medicine of the University of Pennsylvania; Dr. Wilfred E. Fry, Assistant Professor of Ophthalmology at the University of Pennsylvania; Dr. Alfred Cowan, Associate Professor of Ophthalmology of the Graduate School of Medicine of the University of Pennsylvania; Dr. William Thornwall Davis, Professor of Ophthalmology at George Washington School of Medicine; Dr. Charles Blassingame, Clinical Associate in the Department of Otolaryngology of the University of Tennessee; Dr. James A. Babbitt, Associate Professor of Otolaryngology at the Graduate School of Medicine of the University of Pennsylvania; Dr. Edwin Broyles, Associate in Laryngology at Johns Hopkins Medical School; Dr. Oscar Swineford, Assistant Professor of Medicine at the University of Virginia Medical School; and Dr. H. B. Mulholland, Professor of the Practice of Medicine at the University of Virginia Medical School. The number who registered for the course was forty-five.

Dr. John P. Peters, Professor of Medicine at Yale University School of Medicine, gave the first Alpha Omega Alpha address for the session on December 11. His subject was Social Implications of Medical Science.

Progress in Syphilis Control.

According to the U. S. Public Health Service, approximately 103,000 patients were discharged from clinics as cured or with syphilis arrested in 1939, as compared with 78,000 in 1938. Almost 60 per cent more persons were brought under treatment for the first time in 1939 than in 1938. The number of treatments increased from 5,200,000 in 1938 to 8,000,000 in 1939.

By the close of 1939 the health department of every state and territory had a separate division or subdivision charged with the control of the venereal diseases. In 1938 only twenty-seven states were so organized. Nineteen states now require examinations, including blood tests for syphilis of all applicants for marriage licenses and fifteen states require physicians to perform blood tests for syphilis on expectant mothers.

Dr. W. D. Kendig,

Kenbridge, has been re-elected chairman of the Lunenburg County Democratic Committee for 1940.

Promotions in National Guard.

Dr. Wilbur R. Southward, Richmond, of the Medical Corps First Virginia Infantry, has been promoted to major and assigned to duty with the Headquarters Second Battalion, 104th Medical Regiment, a unit recently allocated to Virginia.

Dr. Frederick P. Barrow, II, Portsmouth, of the Medical Corps, 111th Field Artillery, has been promoted to major of the medical detachment, succeeding Major George W. Schenck, Norfolk, resigned.

Doctors Work with Boy Scout Group.

Dr. John Hundley, Jr., has been re-elected vice-chairman of the Lynchburg Area Boy Scout Group

and Dr. John W. Devine, Jr., also of Lynchburg, was elected district commissioner.

Bequests for Research.

Gifts of approximately $1,500,000 to Northwestern University and of approximately $1,000,000 to the University of Chicago are announced by the Trustees of the Estate of Clara A. Abbott, who died in 1924, and whose will is now finally closed. Both gifts will be used for medical and chemical research.

The gift to the University of Chicago will operate to secure for that Institution an additional $1,500,000 from the Rockefeller Foundation to be used for Biological Research which was promised conditionally upon the University securing an additional amount now realized by the Abbott Estate gift.

Mrs. Abbott was the widow of Dr. Wallace C. Abbott, Founder of Abbott Laboratories, who was a practicing physician in Chicago for many years and began the manufacture of chemicals and pharmaceuticals in Ravenswood, Ill., in 1888. Both were much interested in research work in colleges and universities.

Other gifts included the following approximate amounts to: Victory Memorial Hospital, Waukegan, Ill., $250,000; Evanston Hospital, Evanston, Ill., $250,000; and Knox College, Galesburg, Ill., $250,000.

Dr. Harry J. Warthen, Jr.,

Richmond, was elected to membership in the Southern Surgical Association at its recent meeting in Augusta, Ga.

Dr. L. G. Roberts,

Moormans River, was recently elected chairman of the Democratic Committee of the district composed of the City of Charlottesville and the counties of Albemarle, Greene, Madison, and Fluvanna.

The Eighth American Scientific Congress

Will be held in Washington, D. C., may 10 to 18, 1940, under the auspices of the Government of the United States of America. By special Act of Congress, invitations have been extended to the Governments of the American Republics members of the Pan American Union to participate in this meeting. The Congress will be divided into eleven sections, one of which will be devoted to Public Health and Medicine. Dr. Alexander Wetmore, assistant secretary of the Smithsonian Institution, has been designated Secretary General of the Congress.

Southern Surgical Association.

At the annual meeting of the Association in Augusta, Ga., early in December, the following officers were elected: President, Dr. John Staige Davis, Baltimore; vice-presidents, Drs. W. L. Peple, Richmond, and W. A. Bryan, Nashville; secretary, Dr. Alton Ochsner, New Orleans; and treasurer, Dr. C. A. Vance, Lexington, Ky. The last two were re-elected. The next meeting will be at Hot Springs, Va.

Dr. M. T. Rosser,

Who recently practiced at Hillsville, is now on active duty with the Navy, with the rank of Lieutenant-Commander, MC-USNR, and is stationed at Parris Island, S. C.

Dr. J. O. Fitzgerald, Jr.,

Richmond, was elected president of the Camera Club of this city, at its annual meeting early in December.

Dr. Guy Hinsdale,

White Sulphur Springs, W. Va., was recently elected president of the Greenbrier Valley (W. Va.) Medical Society. Dr. D. G. Lewis of Lewisburg is vice-president, and Dr. A. G. Lanham of Ronceverte is secretary.

Mt. Regis Sanatorium Closed.

Dr. Everett E. Watson, for the past twenty-six years medical director of Mt. Regis Sanatorium at Salem, announces the closing of that institution. He, however, will continue to make his home at the sanatorium, and will devote his entire time to consultations by appointment. While his offices, laboratory and X-ray laboratory will be at the former sanatorium, he will continue to see out-patients also.

Dr. James H. Smoot,

Woodstock, has been re-elected president of the Shenandoah County Fair Association.

The National Conference on Medical Service,

Formerly the Northwest Regional Conference, will hold its 14th annual meeting at the Palmer House, Chicago, Sunday, February 11, 1940. All state medi-

cal societies have been invited to send representatives to the Conference, designed to provide a medium for the verbal exchange of information on progressive medical service activities being conducted throughout the United States, and to discuss the solution of problems arising from the distribution of medical service to all classes. The Conference is not official nor political, is not connected with any other organization or committee, and its deliberations result in no resolutions or motions. It is informal, has no dues, by-laws, or formal organizational structure. Seventeen men, representing as many states in the Union, will be on the program of this one-day meeting.

L. Fernald Foster, M.D., Bay City, Michigan, is president of the National Conference; and Forrest L. Loveland, M.D., Topeka, Kansas, is secretary.

Dr. William B. Wilkins,

Recently of Alexandria, has moved to West Palm Beach, Fla., and has offices in Suite 715 Harvey Building. He will limit his practice to internal medicine with especial reference to cardiology.

Dr. Edw. Valentine Jones, Jr.,

Class of '35, University of Virginia, Department of Medicine, recently connected with health work at Logan, W. Va., is now at the School of Hygiene and Public Health, Johns Hopkins University, Baltimore, where he is a candidate for the degree of Master of Public Health. Upon completion of this course, he will return to Logan to be engaged in syphilis control work under the direction of the West Virginia State Health Department.

New Unit Opened at Sanatorium.

The new infirmary and culinary building at Blue Ridge Sanatorium, Charlottesville, erected at a cost of $275,000, exclusive of furnishings, has been completed and was opened to inspection on the afternoon of December 17. It is the major unit of a project which is to include a new central heating plant and the remodelling of the old culinary department into nurses' quarters. This will increase the capacity of the sanatorium by approximately 100 beds.

Drs. Cary and Helvestine.

Dr. S. Beverly Cary of Roanoke announces the association of Dr. Frank Helvestine, Jr. They have offices in Suite 303 Medical Arts Building, and will limit their practice to urology.

Dr. James N. Williams,

Director of the Virginia State Bureau of Mental Hygiene, was the guest speaker before the Pediatric Section of the Norfolk County Medical Society on November 27.

Dr. Paul McBee,

An alumnus of the Medical College of Virginia, class of '30, recently located at Bakersville, N. C., has moved to Marion, that State. He will limit his work to surgery at the Marion General Hospital, with which he has been connected on the surgical staff for six years.

Officers of Ruritan Club.

Dr. E. B. Pendleton, Cuckoo, was recently elected president of the Louisa County Ruritan Club. Dr. H. G. Byrd, Louisa, was made director for a one-year term.

Wanted for Temporary Work.

Physician wanted to take over practice of a physician in western part of State for month of February. Address "T", care the VIRGINIA MEDICAL MONTHLY. (*Adv.*)

Will Sell or Rent—

Office equipment, including complete X-ray and accessories, of physician who is discontinuing practice. Will rent four room office, heated, with water and lights, to one who wishes this location in modern town of 700 to 800 inhabitants, all white, and 2,000 to 3,000 in immediate vicinity. Improved roads; no other doctor in town. If interested, address "Office and Practice", care this JOURNAL. (*Adv.*)

For Sale—

Burdick Standard Quartz Mercury Treatment lamp. First class condition. Price reasonable. For further information address "No. 175", care this JOURNAL. (*Adv.*)

Wanted—

Good used short wave diathermy machine, sub stage lamp, electric centrifuge, Spencer bright line hemacytometer, Vim sheftel colorimeter, and other physician's laboratory equipment. Must be in perfect condition and reasonable. Address "Scope", care VIRGINIA MEDICAL MONTHLY, Richmond. (*Adv.*)

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Obituary Record

Dr. Rudolph Angus Nichols, Jr.,

Prominent Richmond physician, died December 10, following a heart attack, though he was apparently in good health earlier that day. He was thirty-nine years of age and a graduate of the University of Virginia, Department of Medicine, in 1926. Dr. Nichols was a member of the faculty of the Medical College of Virginia. He was also a member of Phi Beta Pi medical fraternity, the Richmond Rotary Club, and the Medical Society of Virginia. He is survived by his wife, his father, Dr. R. A. Nichols, Sr., a brother and a sister.

Dr. Austin Micklem,

Of Rockfish, died November 23, at the University of Virginia Hospital after a short illness, and was buried at Riverside Presbyterian Church at Rockfish. He was born in Berkshire, England, and graduated in pharmacy there, but as a young man he came to America and graduated from the Medical College of Virginia, Richmond, in 1891. He was eighty-one years old at his death and was a member of the Nelson County Medical Society and the Medical Society of Virginia. His wife and several children survive him.

At a called meeting of the Nelson County Medical Society the following resolutions were adopted:

WHEREAS, an Ever Wise Providence has removed from our membership our beloved Colleague, who for many years has been greatly beloved by us and those among whom he practiced, because of his attractive personality, kind and sympathetic manner, his fine ideals and loyal sense of sincerity, for which we shall always revere his memory;

BE IT RESOLVED, That in his death the medical profession or our community has sustained a great loss;

BE IT FURTHER RESOLVED, That we tender our sympathy to the family of our deceased associate in this bereavement;

BE IT FURTHER RESOLVED, That a copy of these resolutions be spread upon the minutes of our association, a copy be sent to the family, and to the VIRGINIA MEDICAL MONTHLY and *The Charlottesville Progress.*

E. C. KIDD,
F. M. HORSLEY, *Chairman.*

Dr. Bertrand Ryland Hudnall,

For many years a prominent physician of Covington, died December 21, as the result of a heart attack following pneumonia. He graduated in medicine from the Medical College of Virginia in Richmond in 1899, and had been a member of the Medical Society of Virginia for thirty-five years. Surviving are his wife and three children, one of them Dr. Harry G. Hudnall of Covington. Dr. R. L. Hudnall of Reedville is a brother.

Dr. James Jett McCormick,

Norfolk, died December 21, after a long illness. He was a native of Clarke County, and seventy-one years of age. His degree in medicine was received from the University of Virginia in 1892. He practiced for a number of years in Norfolk, before being made city health commissioner in 1931. His widow survives him.

Resolutions on Dr. J. Lewis Rawls.

The following resolutions were adopted by the Executive Committee of the Virginia Tuberculosis Association at its meeting on December 7, 1939:

WHEREAS, The Virginia Tuberculosis Association has sustained a great loss in the death of Dr. John Lewis Rawls, of Suffolk, who was killed in an automobile accident on September 4, 1939, and,

Since Dr. Rawls was an earnest and devoted member of the Board of Directors, therefore be it

RESOLVED that the Executive Committee of the Association at this, its first meeting since his death, record their profound regret at his untimely death, and be it

FURTHER RESOLVED, that these resolutions be spread upon the minutes of the Association and a copy sent to his family.

Resolutions on Dr. Antonio Gentile.

WHEREAS, Providence has removed from our midst our colleague, Dr. Antonio Gentile, who in a comparatively few years among us had earned the love and admiration of his associates and whose knowledge of his profession commanded the respect of all;

BE IT RESOLVED, That in his death, the medical profession has lost an able colleague; the community, a friend and kind physician;

BE IT FURTHER RESOLVED, That we tender our sympathy to the family of our deceased colleague in their sorrow.

BE IT FURTHER RESOLVED, That a copy of these resolutions be spread upon the minutes of our Academy of Medicine, a copy sent to the family, and to the VIRGINIA MEDICAL MONTHLY.

R. A. DAVIS,
E. B. MEWBORNE,
J. E. MARABLE, *Chairman.*